Foley, S.
09/500904

Seq.s claim 8
Seq. IDs 1-39
7

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     FILE 'REGISTRY' ENTERED AT 14:32:36 ON 06 DEC 2000
L1          101 SEA ABB=ON  PLU=ON  PPPGRRP|GRGRGRGG|RGRGREK|GAGAGAGAGAGA
                GAGAGAGAGAGA/SQSP

     FILE 'CAPLUS' ENTERED AT 14:33:40 ON 06 DEC 2000
L2           61 SEA ABB=ON  PLU=ON  L1
L3           15 SEA ABB=ON  PLU=ON  L2 AND (EB OR EPSTEIN BARR)

E1 THROUGH E24 ASSIGNED

=> d 1-15 .bevstr; fil reg; s e1-e24

L3   ANSWER 1 OF 15  CAPLUS  COPYRIGHT 2000 ACS
ACCESSION NUMBER:         2000:573970  CAPLUS
DOCUMENT NUMBER:          133:172998
TITLE:                    Stabilization of intact episomes in eukaryotic
                          cells using balanced pairs of markers
INVENTOR(S):              Horlick, Robert A.; Chelsky, Daniel
PATENT ASSIGNEE(S):       Pharmacopeia, Inc., USA
SOURCE:                   PCT Int. Appl., 53 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2000047778      A1   20000817       WO 2000-US3547   20000211
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
             CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
             ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                    US 1999-249585   19990211
AB   A method for obtaining a eukaryotic cell transfected with an episome
     involves transfecting the cell with the episome under conditions
     wherein cells that survive are successfully transfected with the
     episome.  The resulting cells express both a first protein whose
     expression causes cell death and second protein whose expression
     prevents cell death resulting from expression of the first protein.
     The method avoids the need for conventional selection methods, such
     as antibiotics.
IT   288332-56-9
     RL: PRP (Properties)
```

(unclaimed sequence; stabilization of intact episomes in eukaryotic cells using balanced pairs of markers)

REFERENCE COUNT: 6

REFERENCE(S):
(2) Horlick; US 5976807 A 1999 CAPLUS
(3) Horlick; Gene 2000, V243(1-2), P187 CAPLUS
(4) Kinsella; Human Gene Therapy 1996, V7, P1405 CAPLUS
(5) Medical Research Council; WO 9807876 A2 1998 CAPLUS
(6) Muecke; Gene Therapy V4(2), P82 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:704902 CAPLUS

DOCUMENT NUMBER: 131:332985

TITLE: Use of viral replication functions to promote stable transformation of eukaryotic cells with multiple autonomously replicating episomes

INVENTOR(S): Horlick, Robert A.; Damaj, Bassam B.; Robbins, Alan K.

PATENT ASSIGNEE(S): Pharmacopeia, Inc., USA

SOURCE: U.S., 47 pp., Cont.-in-part of U.S. Ser. No. 40,961.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5976807	A	19991102	US 1998-130114	19980806
WO 9947647	A1	19990923	WO 1999-US3307	19990212
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9927679	A1	19991011	AU 1999-27679	19990212
PRIORITY APPLN. INFO.:			US 1998-40961	19980318
			US 1998-130114	19980806
			WO 1999-US3307	19990212

AB A method is described for the efficient generation of eukaryotic cell lines carrying several genes of interest on independently replicating episomes. This allows the use of multiple independent

vectors, e.g. in the study or manuf. of multisubunit proteins. The method uses viral replication functions, specifically the replication origin of **Epstein-Barr** virus and the viral antigen EBNA1, with one vector carrying the origin of replication and the EBNA1 gene and the other carrying the origin and a selectable marker gene. Only cells carrying both plasmids will survive selection. Use of the method to construct signal transduction chains of G proteins and G protein coupled receptors is demonstrated. Cell lines in which the genes were stable expressed at the same level for up to six months, with the signal transduction chains showing the expected properties were obtained.

IT **244168-99-8**
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid sequence; use of viral replication functions to promote stable transformation of eukaryotic cells with multiple autonomously replicating episomes)

REFERENCE COUNT: 1
REFERENCE(S): (1) Horlick; Prot Expr and Purif 1997, V9, P301 CAPLUS

L3 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:614090 CAPLUS
DOCUMENT NUMBER: 131:238810
TITLE: Use of viral replication functions to promote stable transformation of eukaryotic cells with multiple autonomously replicating episomes
INVENTOR(S): Horlick, Robert A.; Robbins, Alan K.; Damaj, Bassam B.
PATENT ASSIGNEE(S): Pharmacopeia, Inc., USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9947647	A1	19990923	WO 1999-US3307	19990212

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,

CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 5976807	A	19991102	US 1998-130114	19980806
AU 9927679	A1	19991011	AU 1999-27679	19990212
PRIORITY APPLN. INFO.:			US 1998-40961	19980318
			US 1998-130114	19980806
			WO 1999-US3307	19990212

AB A method is described for the efficient generation of eukaryotic cell lines carrying several genes of interest on independently replicating episomes. This allows the use of multiple independent vectors, e.g. in the study or manuf. of multisubunit proteins. The method uses viral replication functions, specifically the replication origin of **Epstein-Barr** virus and the viral antigen EBNA1, with one vector carrying the origin of replication and the EBNA1 gene and the other carrying the origin and a selectable marker gene. Only cells carrying both plasmids will survive selection. Use of the method to construct signal transduction chains of G proteins and G protein coupled receptors is demonstrated. Cell lines in which the genes were stable expressed at the same level for up to six months, with the signal transduction chains showing the expected properties were obtained.

IT **244168-99-8**
RL: BPR (Biological process); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid sequence; use of viral replication functions to promote stable transformation of eukaryotic cells with multiple autonomously replicating episomes)

REFERENCE COUNT: 1
REFERENCE(S): (1) Horlick, R; Protein Expression and Purification 1997, V9, P301 CAPLUS

L3 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:536243 CAPLUS
DOCUMENT NUMBER: 131:282246
TITLE: Inhibition of antigen presentation by the glycine/alanine repeat domain is not conserved in simian homologues of **Epstein-Barr** virus nuclear antigen 1
AUTHOR(S): Blake, Neil W.; Moghaddam, Amir; Rao, Pasupuleti; Kaur, Amitinder; Glickman, Rhona; Cho, Young-Gyu; Marchini, Andrew; Haigh, Tracey; Johnson, R. Paul; Rickinson, Alan B.; Wang, Fred
CORPORATE SOURCE: CRC Institute for Cancer Studies, University of Birmingham Medical School, Birmingham, B15 2TA, UK
SOURCE: J. Virol. (1999), 73(9), 7381-7389
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Most humans and Old World nonhuman primates are infected for life with **Epstein-Barr** virus (EBV) or closely related gammaherpesviruses in the same lymphocryptovirus (LCV) subgroup. Several potential strategies for immune evasion and persistence have been proposed based on studies of EBV infection in humans, but it has been difficult to test their actual contribution exptl. Interest has focused on the EBV nuclear antigen 1 (EBNA1) because of its essential role in the maintenance and replication of the episomal viral genome in latently infected cells and because EBNA1 endogenously expressed in these cells is protected from presentation to the major histocompatibility complex class-I restricted cytotoxic T-lymphocyte (CTL) response through the action of an internal glycine-alanine repeat (GAR). Given the high degree of biol. conservation among LCVs which infect humans and Old World primates, we hypothesized that strategies essential for viral persistence would be well conserved among viruses of this subgroup. We show that the rhesus LCV EBNA1 shares sequence homol. with the EBV and baboon LCV EBNA1 and that the rhesus LCV EBNA1 is a functional homolog for EBV EBNA1-dependent plasmid maintenance and replication. Interestingly, all three LCVs possess a GAR domain, but the baboon and rhesus LCV EBNA1 GARs fail to inhibit antigen processing and presentation as detd. by using three different in vitro CTL assays. These studies suggest that inhibition of antigen processing and presentation by the EBNA1 GAR may not be an essential mechanism for persistent infection by all LCV and that other mechanisms may be important for immune evasion during LCV infection.

IT **246242-20-6**
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(amino acid sequence; inhibition of antigen presentation by glycine/alanine repeat domain not conserved in simian homologs of EBNA-1 antigen)

IT **180514-60-7**, Protein EBNA1 (herpesvirus papio strain 594-S clone p701)
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(inhibition of antigen presentation by glycine/alanine repeat domain not conserved in simian homologs of EBNA-1 antigen)

REFERENCE COUNT: 39

REFERENCE(S):
(1) Allen, T; J Immunol 1998, V160, P6062 CAPLUS
(2) Blake, N; Immunity 1997, V7, P791 CAPLUS
(3) Blasco, R; Gene 1995, V158, P157 CAPLUS
(4) Falk, K; J Gen Virol 1995, V76, P779 CAPLUS
(5) Franken, M; J Virol 1995, V69, P8011 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:184278 CAPLUS

DOCUMENT NUMBER: 130:222117
TITLE: Methylated, SmD homologous peptides, reactive with the antibodies from sera of living beings affected with systemic lupus erythematosus
INVENTOR(S): Meheus, Lydie; Luhrmann, Reinhard Georg; Union, Ann; Raymackers, Joseph
PATENT ASSIGNEE(S): Innogenetics N.V., Belg.
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911667	A1	19990311	WO 1998-EP5518	19980831
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9894387	A1	19990322	AU 1998-94387	19980831
EP 944649	A1	19990929	EP 1998-947487	19980831
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: EP 1997-870127 19970829
WO 1998-EP5518 19980831

AB The present invention relates to a method of producing certain peptides contg. methylated arginines that are followed by a glycine residue and that constitute immunogenic determinants of antibodies present in sera from patients with systemic lupus erythematosus, or **Epstein-Barr** virus and wherein the methylation is a prerequisite for reacting with said antibodies. The invention also relates to the use of said peptides for diagnosis and treatment of systemic lupus erythematosus and related diseases, and diseases in which **Epstein-Barr** virus has been implicated.
In addn., immunotoxin of the methylated SmD peptide-specific monoclonal antibody and antiidiotype antibody are also disclosed for diagnosis and treatment of autoimmune diseases and **Epstein -Barr** virus-related diseases.

IT **221116-56-9 221116-74-1 221130-89-8 221130-93-4**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methylated SmD homologous peptides, antibodies and antiidiotype antibodies for diagnosis and treatment of autoimmune and **Epstein-Barr** virus-assocd. diseases)

REFERENCE COUNT: 5

REFERENCE(S):
(1) Neosystem Sa; WO 9118920 A 1991
(2) Rawal, N; BIOCHIMICA AND BIOPHYSICA ACTA 1995, V1248, P11 CAPLUS
(3) Rokeach, L; PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA 1988, V85, P4832 CAPLUS
(4) Scripps Clinic Res; WO 8601210 A 1986
(5) Univ Duke; WO 9513805 A 1995

L3 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:490661 CAPLUS
DOCUMENT NUMBER: 129:135181
TITLE: Diagnostics and therapy of **Epstein-Barr** virus in autoimmune disorders
INVENTOR(S): Harley, John B.; James, Judith A.
PATENT ASSIGNEE(S): Oklahoma Medical Research Foundation, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9830586	A2	19980716	WO 1998-US342	19980113
WO 9830586	A3	19981217		
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9860185	A1	19980803	AU 1998-60185	19980113
EP 1007552	A2	20000614	EP 1998-903405	19980113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-781296 19970113
WO 1998-US342 19980113

AB Data consistent with autoimmune disease being caused by **Epstein-Barr** virus are shown. Based on this evidence, an effective vaccine would prevent the autoimmune disease in those vaccinated, modified or administered so that the vaccine is not itself capable of inducing autoimmune disease. In the case of anti-Sm, structures to be avoided in **Epstein-Barr** virus-derived vaccine have been identified. Differences have been identified in the immune responses to **Epstein-Barr** infection between individuals who develop a specific autoimmune

disease and those who do not. These differences are used to distinguish those who are at greater risk for developing specific autoimmune diseases from those who are at lesser risk. Assuming **Epstein-Barr** virus causes autoimmune disease and that **Epstein-Barr** virus remains latent in the patient for life, reactivation of the virus from the latent state is important in generating or maintaining the autoimmune response that culminates in autoimmune disease. Cells infected with latent virus may also encourage autoimmunity. Based on the understanding that reactivation or latency are important to produce or sustain autoimmunity, then therapies directed against **Epstein-Barr** virus will also be effective therapies for the autoimmune manifestations of disease for which **Epstein-Barr** virus is responsible.

IT **192565-50-7 210571-88-3 210571-89-4 210571-91-8 210571-92-9 210572-01-3**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapy of **Epstein-Barr** virus in autoimmune disorders)

L3 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:432545 CAPLUS
DOCUMENT NUMBER: 127:107913
TITLE: Lupus humoral autoimmunity after short peptide immunization
AUTHOR(S): James, Judith A.; Scofield, R. Hal; Harley, John B.
CORPORATE SOURCE: Arthritis and Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 73104, USA
SOURCE: Ann. N. Y. Acad. Sci. (1997), 815(B Lymphocytes and Autoimmunity), 124-127
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two rabbits were immunized with a peptide derived from the EBNA-1 antigen of **Epstein-Barr** virus that is very similar to a peptide from the Sm B/B' antigen. Both animals mounted an immune response to the peptide of immunization and also initially against the peptide from Sm B/B'. In one animal, these antibodies appear to be cross-reactive with Sm, leading to the capacity to present this autoantigen (via class II) and then to develop lupus autoimmunity. The other animal, however, developed only peptide-specific antibodies and its immune response never became directed against the whole Sm protein. These observations are consistent with the paradigm previously offered for the crit. events in human lupus from antigenically cross-reactive intact structure to

presentation to autoimmunity (J. A. T. James, et al., 1995).

IT **192565-50-7**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(lupus humoral autoimmunity after short peptide immunization)

L3 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:484294 CAPLUS
DOCUMENT NUMBER: 125:161490
TITLE: Comparison of the EBNA1 proteins of **Epstein-Barr** virus and herpesvirus papio in sequence and function
AUTHOR(S): Yates, John L.; Camiolo, Sarah M.; Ali, Sayed; Ying, Angela
CORPORATE SOURCE: Dep. Human Genetics, Roswell Park Cancer Inst., Buffalo, NY, 14263, USA
SOURCE: Virology (1996), 222(1), 1-13
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The EBNA1 protein of **Epstein-Barr** virus (EBV) supports replication and maintenance of the circularized viral chromosome in cells that are latently infected. We have isolated, sequenced, and functionally characterized the EBNA1 gene of herpesvirus papio (HVP), an EBV-like virus that infects baboons. The amino acid sequences of EBNA1 of HVP and EBV are 56% identical, if the difference in the length of the glycine and alanine contg. repetitive region, which is much shorter for HVP EBNA1, is omitted for the calcn. The key structural features of the DNA-binding/dimerization domain (the carboxyl-terminal domain) appear to have been conserved, as have amino acids in the two regions thought to be most crit. for DNA binding. Most of the salient features of the amino-terminal two-thirds of EBNA1 (the amino-terminal domain), including a dearth of sequences predictive of alpha-helical or beta-sheet structures, are shared by the two sequences, although numerous gaps in this region were needed for alignment of the sequences. The amino-terminal fifty amino acids of EBNA1 of both EBV and HVP weakly resemble the amino terminus of rat ribosomal protein S2. Plasmids carrying oriP of either virus replicated stably in mammalian cells and supported efficient outgrowth of colonies under selection when supported by EBNA1 from either virus, although with each oriP there was a noticeable preference for EBNA1 to be from the same virus. HVP EBNA1 was less effective than EBV EBNA1 at activating the enhancer function of EBV oriP and under certain conditions was less effective than EBV EBNA1 at supporting maintenance of plasmids carrying EBV oriP. Results obtained with hybrid EBNA1 mols. indicated that differences in the amino-terminal and carboxyl-terminal domains, resp., are primarily responsible for the differences in transcriptional activation and

plasmid maintenance, resp. The results showed that changes within EBNA1 can differentially alter its transcriptional and replicational activities.

IT **180514-60-7**
RL: PRP (Properties)
(amino acid sequence; comparison of the EBNA1 proteins of **Epstein-Barr** virus and herpesvirus papio in sequence and function)

L3 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:265322 CAPLUS
DOCUMENT NUMBER: 124:315052
TITLE: Purification of **Epstein-Barr** virus nuclear antigen 1 for diagnostic use and cloning and expression of the gene
INVENTOR(S): O'Donnell, Michael E.
PATENT ASSIGNEE(S): Cornell Research Foundation, Inc., USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9602563	A1	19960201	WO 1995-US8700	19950713
W: JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 770090	A1	19970502	EP 1995-927137	19950713
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:			US 1994-275614	19940713
			WO 1995-US8700	19950713

AB A process for expressing and recovering **Epstein-Barr** nuclear antigen 1 (EBNA1) protein or polypeptide treats cells having a nucleus contg. expressed EBNA1 protein or polypeptide to recover the nucleus contg. the expressed EBNA1 protein or polypeptide. The nucleus contg. the expressed EBNA1 protein or polypeptide is then sepd. into a liq. fraction contg. the expressed EBNA1 protein or polypeptide and a solid fraction contg. substantially all DNA from the nucleus. The liq. fraction is sepd. from the solid fraction, and EBNA1 protein or polypeptide is recovered from the liq. fraction. The method is optimized for purifn. of the antigen from a baculovirus expression system and allows the manuf. of analogs with a near-full-length Gly-Ala repeat. Also encompassed by the present invention is an EBNA1 protein or polypeptide having substantially no components which generate false

pos. readings when used to detect **Epstein-Barr** virus in human serum, the DNA mol. encoding it, and recombinant expression of the protein. The protein is useful in a method for detection of **Epstein-Barr** virus. Purified EBNA1 showed the expected binding characteristics for oriP and the dyad element.

IT **176024-36-5P**
RL: BPN (Biosynthetic preparation); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(amino acid sequence, manuf. in Sf9 cells of; purifn. of **Epstein-Barr** virus nuclear antigen 1 for diagnostic use and cloning and expression of gene)

L3 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:713826 CAPLUS
DOCUMENT NUMBER: 123:110142
TITLE: Diagnostic reagents for the detection of antibodies to **Epstein Barr** Virus
INVENTOR(S): Middeldorp, Jaap Michiel; Van Grunsven, Wouterus Marinus
PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.
SOURCE: Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 649904	A1	19950426	EP 1994-202598	19940909
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2131874	AA	19950315	CA 1994-2131874	19940912
FI 9404225	A	19950315	FI 1994-4225	19940913
AU 9472956	A1	19950330	AU 1994-72956	19940913
AU 679545	B2	19970703		
ZA 9407061	A	19950427	ZA 1994-7061	19940913
JP 07209302	A2	19950811	JP 1994-220488	19940914
US 5827646	A	19981027	US 1994-306078	19940914
PRIORITY APPLN. INFO.:			EP 1993-202659	19930914

AB A diagnostic reagent for the detection of antibodies against **Epstein Barr** Virus is disclosed. The diagnostic reagent comprises a combination of at least part of an EBV structural protein, preferably a viral capsid antigen (VCA) or a membrane antigen (MA), and at least part of an **Epstein Barr** nuclear antigen (EBNA). Preferably, the VCA-protein is

VCA-p18 protein, the MA-protein is MA-gp350/220 protein and the EBNA-protein is EBNA-1 protein. It has been found that the combination of a VCA-protein or a MA-protein, and an EBNA protein, into a single diagnostic assay yields an EBV-antibody detection method with greater sensitivity and accuracy than current methods.

IT **155646-18-7 155981-79-6**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**Epstein Barr** Virus nuclear antigen-1-derived peptide for detection of antibodies to **Epstein Barr** Virus)

IT **155981-78-5**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(for diagnostic reagents for the detection of antibodies to **Epstein Barr** Virus)

L3 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:542901 CAPLUS
DOCUMENT NUMBER: 123:6883
TITLE: Alterations in the structure of the EBV nuclear antigen, EBNA1, in epithelial cell tumors
AUTHOR(S): Snudden, Dee K.; Smith, Paul R.; Lai, Daniel; Ng, Mun-Hong; Griffin, Beverly E.
CORPORATE SOURCE: Dep. Virol., Royal Postgrad. Med. Sch., London, W12 0NN, UK
SOURCE: Oncogene (1995), 10(8), 1545-52
CODEN: ONCNES; ISSN: 0950-9232
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The EBV nuclear antigen, EBNA1, is the only viral protein consistently expressed in all virus-infected cells. It is required in trans for viral replication, maintenance of EBV extrachromosomal episomes, and transcriptional transactivation in latently-infected B-cells. It binds RNA suggestive of a regulatory role in post-transcriptional events and in transgenic mice, it is tumorigenic. In RNase protection studies relating to the EBV-assocd. tumor, nasopharyngeal carcinoma (NPC), the authors show that a C-terminal EBNA1 RNA probe from the prototype B95-8 marmoset strain can protect its own mRNA from enzymic digestion, but does not fully protect EBNA1 mRNA from NPC cells. This finding is consistent with changes in the coding region for the antigen. The authors thus detd. the sequences of EBNA1 genes derived from an NPC xenograft and numerous patient biopsies and identified a no. of mutations in the gene in these human cells, relative to B95-8. Many of the nucleotide changes would lead to non-conservative amino acid alterations in apparently functionally significant regions of the protein. The authors show that although some of the mutations lie in regions designated as crit. to DNA binding, they have negligible

effect on this property of EBNA1. The basic regions in EBNA1 that may bind to RNA, at least in vitro, are exempt from mutation. Thus, unless the alterations are silent, which for such a crit. viral function seems unlikely, they may relate to as yet unmapped viral activities, such as a role in tumorigenesis and the ability of EBNA1 to evade the cellular immune system, or be assocd. with the ability of the antigen to regulate gene transcription.

IT **163753-46-6 163753-47-7 163753-48-8**
RL: PRP (Properties)
(amino acid sequence; sequence of mutated **Epstein-Barr** virus antigen EBNA1 in human nasopharyngeal carcinomas)

L3 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:345529 CAPLUS
DOCUMENT NUMBER: 122:158385
TITLE: Sequential autoantigenic determinants of the small nuclear ribonucleoprotein Sm D shared by human lupus autoantibodies and MRL lpr/lpr antibodies
AUTHOR(S): James, J. A.; Mamula, M. J.; Harley, J. B.
CORPORATE SOURCE: Health Sciences Centre, University of Oklahoma, Oklahoma City, OK, USA
SOURCE: Clin. Exp. Immunol. (1994), 98(3), 419-26
CODEN: CEXIAL; ISSN: 0009-9104
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Autoantibodies directed against the Sm proteins of the spliceosome complex are found in approx. 25% of systemic lupus erythematosus (SLE) patient sera. To det. which regions of the Sm D polypeptide are involved in the lupus autoimmune response, binding to overlapping octapeptides of Sm D has been evaluated with sera from nine Sm D-pos. patients, six patients with other autoimmune serol., and five normal human sera. Lupus patient sera which are Sm precipitin-pos. bind various combinations of five regions of the peptide. The major antigenic region, Epitope 5 (REAVA(GR)10GGPRR), is bound by eight of nine Sm precipitin-pos. sera tested. This region of Sm D shows significant sequence homol. with **Epstein-Barr** nuclear antigen-1. To det. the fine specificity of the murine Sm response, four unique Sm D MoAbs derived from MRL lpr/lpr mice and three adult anti-Sm-pos. MRL lpr/lpr mouse sera have been analyzed. Two of these monoclonals, KSm 4 and Y12, as well as the MRL lpr/lpr sera tested, show binding with Epitope 5. Another of these monoclonals, KSm 2, binds octapeptides 84-91, DVEPKVKSKKREAVAG, which corresponds to Epitope 4 of this study. Antibodies from SLE patients with autoimmune serol. other than anti-Sm bind the carboxyl glycine-arginine repeat (GR)10 peptides of Sm D. However, none of the antibodies tested from patients who do not have lupus and who have different autoimmune

serol. binds any of the Sm D octapeptides. Normal controls did not significantly bind any of the Sm D octapeptides. These results describe two major regions of shared antigenicity of Sm D between sera from SLE patients and MRL lpr/lpr mice, thereby establishing a basis for the cross-species similarity of autoimmunity to the Sm autoantigen in SLE.

IT **161471-45-0**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(epitopes on small nuclear ribonucleoprotein Sm D autoantigen peptides recognized by human lupus autoantibodies and MRL lpr/lpr antibodies)

L3 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1994:433150 CAPLUS
DOCUMENT NUMBER: 121:33150
TITLE: **Epstein-Barr** virus peptides, antibodies against these peptides, and their use for diagnosis
INVENTOR(S): Middeldorp, Jaap Michiel
PATENT ASSIGNEE(S): Akzo N.V., Neth.
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9406912	A1	19940331	WO 1993-EP2478	19930913
W: AU, CA, FI, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 607425	A1	19940727	EP 1993-920714	19930913
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07501710	T2	19950223	JP 1993-507783	19930913
AU 667745	B2	19960404	AU 1993-48162	19930913
FI 9402184	A	19940511	FI 1994-2184	19940511
US 5965353	A	19991012	US 1994-240717	19940511
PRIORITY APPLN. INFO.:			EP 1992-202797	19920914
			WO 1993-EP2478	19930913

AB A synthetic peptide derived from the **Epstein-Barr** nuclear antigen 1 or fragments thereof that are immunochem. reactive with **Epstein-Barr** Virus (EBV) antibodies are provided. A new monoclonal antibody directed to said peptide or fragments thereof is also given. A method for the detection of EBV or anti-EBV antibodies in a test fluid, an immunochem. reagent

comprising the peptide, and a test kit for the method are also disclosed.

IT **155646-18-7**, Antigen (**Epstein-Barr** virus) **155981-78-5**, Antigen (**Epstein-Barr** virus) **155981-79-6**, Antigen (**Epstein-Barr** virus)
RL: PRP (Properties)
(amino acid sequence of, for immunoassay of **Epstein-Barr** virus)

L3 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1994:214717 CAPLUS
DOCUMENT NUMBER: 120:214717
TITLE: Mapping of epitopes on the SmD molecule: the use of multiple antigen peptides to measure autoantibodies in systemic lupus erythematosus
AUTHOR(S): Sabbatini, Alessandra; Dolcher, Maria Pia; Marchini, Barbara; Bombardieri, Stefano; Migliorini, Paola
CORPORATE SOURCE: Clin. Immunol. Unit, Univ. Pisa, Pisa, Italy
SOURCE: J. Rheumatol. (1993), 20(10), 1679-83
CODEN: JRHUA9; ISSN: 0315-162X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Autoantibodies against the ribonucleoproteins B, B' and D are a serol. marker of systemic lupus erythematosus (SLE). The authors mapped the epitopes recognized by autoantibodies on the SmD mol. by 7 synthetic peptides corresponding to the entire length of the protein. By ELISA assay, 25% of the lupus sera contained IgG antibodies specific for the C-terminal SmD sequence 95-119. This reactivity was confirmed by synthesizing the sequence as a multiple antigen peptide (MAP): antibodies reactive with the MAP 95-119 were present only in SLE and not in other connective tissue disorders. Sera contg. high titers of anti-MAP 95-119 antibodies reacted in immunoblot with the SmD protein. These results indicate the presence of a dominant epitope in the C-terminal region of SmD, which is highly homologous to the **Epstein-Barr** virus induced nuclear protein EBNA I.

IT **139444-21-6**
RL: BIOL (Biological study)
(autoantibody binding to, structure in, human lupus erythematosus in relation to)

L3 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1989:52116 CAPLUS
DOCUMENT NUMBER: 110:52116
TITLE: Molecular cloning of a cDNA encoding the human Sm-D autoantigen
AUTHOR(S): Rokeach, Luis A.; Haselby, Jeanne A.; Hoch,

Sallie O.
CORPORATE SOURCE: Agouron Inst., La Jolla, CA, 92037, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1988), 85(13), 4832-6
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Antibodies to the Sm-D polypeptide antigen are closely assocd. with the rheumatic disease systemic lupus erythematosus. Sm-D exists in the cell as one of the core proteins of the small nuclear ribonucleoprotein complexes implicated in RNA processing. A cDNA clone, D45-2, coding for the Sm-D human nuclear antigen was isolated by screening a human B-lymphocyte cDNA library with synthetic oligonucleotide probes. The 1633-base-pair clone contains an open reading frame (ORF) 357 nucleotides long, capable of encoding a 13,282-dalton polypeptide. The Sm-D coding region is initiated at an AUG codon downstream from a sequence with excellent match to the consensus for the eukaryotic ribosome-binding site. The Sm-D ORF is preceded by a 150-nucleotide-long untranslated leader and followed by a 1126-nucleotide-long untranslated region contg. four putative poly(A) signals. The predicted amino acid sequence reveals a (Gly-Arg)9 repeated motif at the C terminus, which may constitute one of the Sm-D immunoreactive determinants. Moreover, this C terminus shows (i) a good homol. to protamines as expected for a nucleic acid binding protein and (ii) a striking similarity to a region in the **Epstein-Barr** nuclear antigen.

IT **118440-43-0**, Antigen Sm-D (human clone D45-2 protein moiety)
RL: PRP (Properties)
(amino acid sequence of)

FILE 'REGISTRY' ENTERED AT 14:35:42 ON 06 DEC 2000
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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STRUCTURE FILE UPDATES: 5 DEC 2000 HIGHEST RN 306933-33-5
DICTIONARY FILE UPDATES: 5 DEC 2000 HIGHEST RN 306933-33-5

TSCA INFORMATION NOW CURRENT THROUGH July 8, 2000

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Structure search limits have been increased. See HELP SLIMIT for details.

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L6 24 SEA FILE=REGISTRY ABB=ON PLU=ON (155646-18-7/BI OR

155981-78-5/BI OR 155981-79-6/BI OR 180514-60-7/BI OR
192565-50-7/BI OR 244168-99-8/BI OR 118440-43-0/BI OR
139444-21-6/BI OR 161471-45-0/BI OR 163753-46-6/BI OR
163753-47-7/BI OR 163753-48-8/BI OR 176024-36-5/BI OR
210571-88-3/BI OR 210571-89-4/BI OR 210571-91-8/BI OR
210571-92-9/BI OR 210572-01-3/BI OR 221116-56-9/BI OR
221116-74-1/BI OR 221130-89-8/BI OR 221130-93-4/BI OR
246242-20-6/BI OR 288332-56-9/BI)

=> s l6 and l1

L7 24 L6 AND L1

=> d 1-24 .bevreg1

L7 ANSWER 1 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **288332-56-9** REGISTRY
CN 17: PN: WO0047778 FIGURE: 2 unclaimed sequence (9CI) (CA INDEX NAME)
CI MAN
SQL 643

SEQ 1 MSDEGPGTGP GNGLGEKGDT SGPEGSGGSG PQRRGGDNHG RGRGRGRGRG
=======
51 GGRPGAPGGS GSGPRHRDGV RRPQKRPSCI GCKGTHGGTG AGAGAGGAGA
=
101 GGAGAGGGAG AGGGAGGAGG AGGAGAGGGA GAGGGAGGAG GAGAGGGAGA
151 GGGAGGAGAG GGAGGAGGAG AGGGAGAGGG AGGAGAGGGA GGAGGAGAGG
201 GAGAGGAGGA GGAGAGGAGA GGGAGGAGGA GAGGAGAGGA GAGGAGAGGA
251 GGAGAGGAGG AGAGGAGGAG AGGGAGGAGA GGGAGGAGAG GAGGAGAGGA
301 GGAGAGGAGG AGAGGGAGAG GAGAGGGGRG RGGSGGRGRG GSGGRGRGGS
351 GGRRGRGRER ARGGSRERAR GRGRGRGRGE KRPRSPSSQS SSSGSPPRRP
=
401 PPGRRPFFHP VGEADYFEYH QEGGPDGEPD VPPGAIEQGP ADDPGEGPST
======
451 GPRGQGDGGR RKKGGWFGKH RGQGGSNPKF ENIAEGLRAL LARSHVERTT
501 DEGTWVAGVF VYGGSKTSLY NLRRGTALAI PQCRLTPLSR LPFGMAPGPG
551 PQPGPLRESI VCYFMVFLQT HIFAEVLKDA IKDLVMTKPA PTCNIRVTVC
601 SFDDGVDLPP WFPPMVEGAA AEGDDGDDGD EGGDGDEGEE GQE

HITS AT: 44-51, 400-406

REFERENCE 1: 133:172998

L7 ANSWER 2 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **246242-20-6** REGISTRY
CN EBNA-1 (antigen) (cercopithecine herpesvirus 15 strain LCL8664) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank U93909-derived protein GI 3342234

```
CI   MAN
SQL  511

SEQ      1 MSDGRGPGNG LGYTGPGLES RPGGASGSGS GGNRGRGAHG RGRGRGRGRG
                                                          =====
        51 RGGGGVLGET GEFGGHGSES ETRHGNGHRD KKRRSCVGCK GGTGGSSAGG
           ===
       101 AGGNSRGGGG AGVGSGRGAG GSGGAGGGAG GSLGGGAGGS SGGSGAGGSG
       151 AGGSGAGGSG AGGSRGRGRG RGGSAGGRGG RGGGGGGGSR GRGRGRGGGS
                           ===== ===                  ========
       201 RGRGRGRGRG RGRGEGPSKG EKRPRSPSGR SSSQSSSRSS SSSRSSSNGS
       251 DSSDFPGFPG HRPLPTSFPG SPLGGYRGTD GTDGGDEQPP GAVEQGPGED
       301 PGEGPSRQTT TSGGRGSGKK GGWFGRRRGE GGRGFKKFEN MAKNLKVLLA
       351 RCQAERTNTT GNWPFGVFVY GPKTSCYNLR RCIACCIPEC RLTPLGRLPF
       401 GYAPEPGPQP GPMRESTDCY FIVFLQTMIF AECVKDALRD YIMTKPLPTS
       451 SVQVTVITFE DPVMLPVFFP PHLPAAAVAA EGGEGAEGDD GDEGGEGGDG
       501 NEGDEGAAGQ E
HITS AT:   46-53, 166-173, 191-198

REFERENCE   1:  131:282246

L7   ANSWER 3 OF 24  REGISTRY  COPYRIGHT 2000 ACS
RN   244168-99-8  REGISTRY
CN   Antigen EBNA 1 (Epstein-Barr virus-associated nuclear antigen 1)
     (human herpesvirus 4) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   EBNA-1 (antigen) (human herpesvirus 4 gene EBNA-1)
CN   PN: WO9947647 FIGURE: 2a claimed protein
CI   MAN
SQL  641

SEQ      1 MSDEGPGTGP GNGLGEKGDT SGPEGSGGSG PQRRGGDNHG RGRGRGRGRG
                                                       =======
        51 GGRPGAPGGS GSGPRHRDGV RRPQKRPSCI GCKGTHGGTG AGAGAGGAGA
           =
       101 GGAGAGGGAG AGGGAGGAGG AGGAGAGGGA GAGGGAGGAG GAGAGGGAGA
       151 GGGAGGAGAG GGAGGAGGAG AGGGAGAGGG AGGAGAGGGA GGAGGAGAGG
       201 GAGAGGAGGA GGAGAGGAGA GGGAGGAGGA GAGGAGAGGA GAGGAGAGGA
       251 GGAGAGGAGG AGAGGAGGAG AGGGAGGAGA GGGAGGAGAG GAGGAGAGGA
       301 GGAGAGGAGG AGAGGGAGAG GAGAGGGGRG RGGSGGRGRG GSGGRGRGGS
       351 GGRRGRGTER ARGGSRERAR GRGRGRGEKR PRSPSSQSSS SGSPPRRPPP
                                                             ===
       401 GRRPFFHPVG EADYFEYHQE GGPDGEPDVP PGAIEQGPAD DPGEGPSTGP
           ====
       451 RGQGDGGRRK KGGWFGKHRG QGGSNPKFEN IAEGLRALLA RSHVERTTDE
       501 GTWVAGVFVY GGSKTSLYNL RRGTALAIPQ CRLTPLSRLP FGMAPGPGPQ
       551 PGPLRESIVC YFMVFLQTHI FAEVLKDAIK DLVMTKPAPT CNIRVTVCSF
       601 DDGVDLPPWF PPMVEGAAAE GDDGDDGDEG GDGDEGEEGQ E
HITS AT:   44-51, 398-404
                           Searcher   :    Shears   308-4994
```

REFERENCE 1: 131:332985

REFERENCE 2: 131:238810

L7 ANSWER 4 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **221130-93-4** REGISTRY
CN L-Arginine, L-.alpha.-aspartyl-L-valyl-L-.alpha.-glutamyl-L-prolyl-L-lysyl-L-valyl-L-lysyl-L-seryl-L-lysyl-L-lysyl-L-arginyl-L-.alpha.-glutamyl-L-alanyl-L-valyl-L-alanylglycyl-N5-[(dimethylamino)iminomethyl]-L-ornithylglycyl-N5-[(dimethylamino)iminomethyl]-L-ornithylglycyl-N5-[(dimethylamino)iminomethyl]-L-ornithylglycyl-N5-[(dimethylamino)iminomethyl]-L-ornithylglycyl-N5-[(dimethylamino)iminomethyl]-L-ornithylglycyl-N5-[(dimethylamino)iminomethyl]-L-ornithylglycyl-N5-[(dimethylamino)iminomethyl]-L-ornithylglycyl-N5-[(dimethylamino)iminomethyl]-L-ornithylglycylglycyl-L-prolyl-L-arginyl- (9CI) (CA INDEX NAME)
CI MAN
SQL 38

SEQ 1 DVEPKVKSKK REAVAGRGRG RGRGRGRGRG RGRGGPRR
=== =====

HITS AT: 28-35

REFERENCE 1: 130:222117

L7 ANSWER 5 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **221130-89-8** REGISTRY
CN L-Arginine, L-.alpha.-aspartyl-L-valyl-L-.alpha.-glutamyl-L-prolyl-L-lysyl-L-valyl-L-lysyl-L-seryl-L-lysyl-L-lysyl-L-arginyl-L-.alpha.-glutamyl-L-alanyl-L-valyl-L-alanylglycyl-N5-[imino(methylamino)methyl]-L-ornithylglycyl-N5-[imino(methylamino)methyl]-L-ornithylglycyl-N5-[imino(methylamino)methyl]-L-ornithylglycyl-N5-[imino(methylamino)methyl]-L-ornithylglycyl-N5-[imino(methylamino)methyl]-L-ornithylglycyl-N5-[imino(methylamino)methyl]-L-ornithylglycyl-N5-[imino(methylamino)methyl]-L-ornithylglycyl-N5-[imino(methylamino)methyl]-L-ornithylglycylglycyl-L-prolyl-L-arginyl- (9CI) (CA INDEX NAME)
CI MAN
SQL 38

SEQ 1 DVEPKVKSKK REAVAGRGRG RGRGRGRGRG RGRGGPRR
=== =====

Searcher : Shears 308-4994

HITS AT: 28-35

REFERENCE 1: 130:222117

L7 ANSWER 6 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **221116-74-1** REGISTRY
CN Glycine, L-.alpha.-aspartyl-L-asparaginyl-L-histidylglycyl-N5-[(dimethylamino)iminomethyl]-L-ornithylglycyl-N5-[(dimethylamino)iminomethyl]-L-ornithylglycyl-N5-[(dimethylamino)iminomethyl]-L-ornithylglycyl-N5-[(dimethylamino)iminomethyl]-L-ornithylglycylglycyl- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 DNHGRGRGRG RGRGGG
=== =====
HITS AT: 8-15

REFERENCE 1: 130:222117

L7 ANSWER 7 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **221116-56-9** REGISTRY
CN Glycine, L-.alpha.-aspartyl-L-asparaginyl-L-histidylglycyl-N5-[imino(methylamino)methyl]-L-ornithylglycyl-N5-[imino(methylamino)methyl]-L-ornithylglycyl-N5-[imino(methylamino)methyl]-L-ornithylglycyl-N5-[imino(methylamino)methyl]-L-ornithylglycylglycyl- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 DNHGRGRGRG RGRGGG
=== =====
HITS AT: 8-15

REFERENCE 1: 130:222117

L7 ANSWER 8 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **210572-01-3** REGISTRY
CN Glycine, L-arginyl-L-prolyl-L-prolyl-L-prolylglycyl-L-arginyl-L-arginyl-L-prolyl-L-phenylalanyl-L-phenylalanyl-L-histidyl-L-prolyl-L-valylglycyl-L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-L-tyrosyl-L-phenylalanyl-L-.alpha.-glutamyl-L-tyrosyl-L-histidyl-L-glutaminyl-L-.alpha.-glutamyl- (9CI) (CA INDEX NAME)
SQL 25

SEQ 1 RPPPGRRPFF HPVGEADYFE YHQEG
=======

Searcher : Shears 308-4994

HITS AT: 2-8

REFERENCE 1: 129:135181

L7 ANSWER 9 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **210571-92-9** REGISTRY
CN Glycine, glycyl-L-prolyl-L-glutaminyl-L-arginyl-L-arginylglycylglycyl-L-.alpha.-aspartyl-L-asparaginyl-L-histidylglycyl-L-arginylglycyl-L-arginylglycyl-L-arginylglycyl-L-arginylglycylglycylglycylglycyl-L-arginyl-L-prolyl- (9CI) (CA INDEX NAME)
SQL 26

SEQ 1 GPQRRGGDNH GRGRGRGRGR GGGRPG
======= ==

HITS AT: 15-22

REFERENCE 1: 129:135181

L7 ANSWER 10 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **210571-91-8** REGISTRY
CN L-Alanine, glycyl-L-alanylglycyl-L-alanylglycyl-L-alanylglycyl-L-alanylglycyl-L-alanylglycyl-L-alanylglycyl-L-alanylglycyl-L-alanylglycyl-L-alanylglycyl-L-alanylglycyl- (9CI) (CA INDEX NAME)
SQL 24

SEQ 1 GAGAGAGAGA GAGAGAGAGA GAGA
========== ========== ====

HITS AT: 1-24

REFERENCE 1: 129:135181

L7 ANSWER 11 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **210571-89-4** REGISTRY
CN L-Lysine, L-arginylglycyl-L-arginylglycyl-L-arginyl-L-.alpha.-glutamyl- (9CI) (CA INDEX NAME)
SQL 7

SEQ 1 RGRGREK
=======

HITS AT: 1-7

REFERENCE 1: 129:135181

L7 ANSWER 12 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **210571-88-3** REGISTRY
CN Glycine, glycyl-L-arginylglycyl-L-arginylglycyl-L-arginylglycyl- (9CI) (CA INDEX NAME)

SQL 8

SEQ 1 GRGRGRGG
========
HITS AT: 1-8

REFERENCE 1: 129:135181

L7 ANSWER 13 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **192565-50-7** REGISTRY
CN L-Proline, L-prolyl-L-prolyl-L-prolylglycyl-L-arginyl-L-arginyl-
(9CI) (CA INDEX NAME)
SQL 7

SEQ 1 PPPGRRP
=======
HITS AT: 1-7

REFERENCE 1: 129:135181

REFERENCE 2: 127:107913

L7 ANSWER 14 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **180514-60-7** REGISTRY
CN Protein EBNA1 (herpesvirus papio strain 594-S clone p701) (9CI) (CA
INDEX NAME)
OTHER NAMES:
CN GenBank U23857-derived protein GI 775215
CI MAN
SQL 476

SEQ 1 MSDEGPGPNN GLGEKGDTGG GGTRGRGGHG RGRGRGRGRG RGHGGSRGGL
51 GGTGGSGSGT GLGDDGLGPG PRPNKKRRSC VGCKGGSGAR GGTSGGSGAG
101 AGGSGAGAGG SGAGAGGSGA GAGGSGAGAG GSGAGAGGSG AGAGGSGGSR
151 GRGRGRGTGS RGRGRGRGGG SGSSRGRGKH RGRGRGRGRG GGREGEGEHG
======== ======= =
201 KKRPRSPSGG SSSSSSASTR ASSGGSSSGS SPVFPGHNSA PLTVPATPLG
251 GDRGTDRPDG GDEPPGAMGQ GPPDDPGEGP SHRPPGQGGP GGPKKGGWFG
301 VRRGQGGYGS KYEKMAQSLR VLLSRCQVPT TNPEGDWPYA VMVYGPKNSC
351 YNLRRCLGCC VPWCRLTPLS RLPYGHSWGT GPEPTPLMES CVSYFLVFLP
401 TGQSAECVKD ALVDYISTRP QPTSSVKVTF CTFDPPVMLP IFYPPPEAPT
451 GSGAEGGEGA EGDDGNEGDE GEEGQE
HITS AT: 162-169, 184-191

REFERENCE 1: 131:282246

REFERENCE 2: 125:161490

L7 ANSWER 15 OF 24 REGISTRY COPYRIGHT 2000 ACS

RN **176024-36-5** REGISTRY
CN Antigen, EBNA 1 (human herpesvirus 4 clone pVL941/EBNA1 nuclear-associated 1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Antigen, EBNA 1 (Epstein-Barr virus clone pVL941/EBNA1 nuclear-associated 1)
CI MAN
SQL 403

```
SEQ      1 MTGPGNGLGE KGDTSGPEGS GGSGPQRRGG DNHGRGRGRG RGRGGGRPGA
                                                  === =====
        51 PGGSGSGPRH RDGVRRPQKR PSCIGCKGTH GGTGAGAGAG GAGAGGGGRG
       101 RGGSGGRGRG GSGGRRGRGR ERARGGSRER ARGRGRGRGE KRPRSPSSQS
       151 SSSGSPPRRP PPGRRPFFHP VGEADYFEYH QEGGPDGEPD VPPGAIEQGP
                 = ======
       201 ADHPGEGPST GPRGQGDGGR RKKGGWFGKH RGQGGSNPKF ENIAEGLRAL
       251 LARSHVERTT DEGTWVAGVF VYGGSKTSLY NLRRGTALAI PQCRLTPLSR
       301 LPFGMAPGPG PQPGPLRESI VCYFMVFLQT HIFAEVLKDA IKDLVMTKPA
       351 PTCNIRVTVC SFDDGVDLPP WFPPMVEGAA AEGDDGDDGD EGGDGDEGEE
       401 GQE
```

HITS AT: 38-45, 160-166

REFERENCE 1: 124:315052

L7 ANSWER 16 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **163753-48-8** REGISTRY
CN Antigen EBNA 1 (human herpesvirus 4 clone C15 nuclear) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Antigen EBNA 1 (Epstein-Barr virus clone C15 nuclear)
CI MAN
SQL 644

```
SEQ      1 MSDEGPGTGP GNGLGQKEDT SGPDGSSGSG PQRRGGDNHG RGRGRGRGRG
                                                       =======
        51 GGRPGAPGGS GSGPRHRGDV RRPQKRPSCI GCKGTHGGTG GAGAGAGAGA
           =                                           ==========
       101 GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA
           ========== ========== ========== ========== ==========
       151 GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA
           ========== ========== ========== ========== ==========
       201 GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA
           ========== ========== ========== ========== ==========
       251 GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA
           ========== ========== ========== ========== ==========
       301 GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA
           ========== ========== ========== ========== ==========
       351 GAGAGAGAER ARGGSRERAR GRGRGRGEKR PRSPSSQSSS SGSPPRRPPP
           ========                                         ===
```

```
       401 GRRPFFHPVG QADYFEYHQE GGPDGEPDMP PGAIEQGPAD DPGEGPSTGP
           ====
       451 RGQGDGGRRK KGGWFGKHRG QGGSNQKFEN IADGLRTLLA RCHVERTTDE
       501 GTWVAGVFVY GGSKTSLYNL RRGISLAIPQ CRLTPLSRLP FGMAPGPGPQ
       551 PGPLRESIVC YFMVFLQTHI FAEVLKDAIK DLVMPKPAPT CNIKATVCSF
       601 DDGVDLPPWF PPMVEGAAAE GDDGDDGDDG DEGGDGDEGE EGQE
HITS AT:   44-51, 91-358, 398-404

REFERENCE   1:  123:6883

L7   ANSWER 17 OF 24  REGISTRY  COPYRIGHT 2000 ACS
RN   163753-47-7  REGISTRY
CN   Antigen EBNA 1 (human herpesvirus 4 clone NPC nuclear) (9CI)  (CA
     INDEX NAME)
OTHER CA INDEX NAMES:
CN   Antigen EBNA 1 (Epstein-Barr virus clone NPC nuclear)
CI   MAN
SQL  641

SEQ      1 MSDEGPGTGP GNGLGQKEDS SGPEGSGGSG PQRRGGDNHG RGRGRGRGRG
                                                       =======
        51 GGRPGAPGGS GSGPRHRGDV RRPQKRPSCI GCKGTHGGTG GAGAGAGAGA
           =                                           ==========
       101 GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA
           ========== ========== ========== ========== ==========
       151 GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA
           ========== ========== ========== ========== ==========
       201 GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA
           ========== ========== ========== ========== ==========
       251 GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA
           ========== ========== ========== ========== ==========
       301 GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA
           ========== ========== ========== ========== ==========
       351 GAGAGAGAER ARGGSRERAR GRGRGRGEKR PRSPSSQSSS SGSPPRRPPP
           ========                                          ===
       401 GRRPFFHPVG DADYFEYLQE GGPDGEPDVP PGAIEQGPTD DPGEGPSTGP
           ====
       451 RGQGDGGRRK KGGWFGKHRG QGGSNPKFEN IAEGLRVLLA RSHVERTTEE
       501 GNWVAGVFVY GGSKTSLYNL RRGIALAVPQ CRITPLSRLP FGMAPGPGPQ
       551 PGPLRESIVC YFMVFLQTHI FAEVLKDAIK DLVMIKPAPT CNIKVTVCSF
       601 DDGVDLPPWF PPMVEGAAAE GDDGDDGDEG GDGDEGEEGQ E
HITS AT:   44-51, 91-358, 398-404

REFERENCE   1:  123:6883

L7   ANSWER 18 OF 24  REGISTRY  COPYRIGHT 2000 ACS
RN   163753-46-6  REGISTRY
CN   Antigen EBNA 1 (human herpesvirus 4 clone B95-8 nuclear) (9CI)  (CA
     INDEX NAME)
```

```
OTHER CA INDEX NAMES:
CN   Antigen EBNA 1 (Epstein-Barr virus clone B95-8 nuclear)
CI   MAN
SQL  641

SEQ      1 MSDEGPGTGP GNGLGEKGDT SGPEGSGGSG PQRRGGDNHG RGRGRGRGRG
                                                        =======
        51 GGRPGAPGGS GSGPRHRGDV RRPQKRPSCI GCKGTHGGTG GAGAGAGAGA
           =                                            ==========
       101 GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA
           ========== ========== ========== ========== ==========
       151 GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA
           ========== ========== ========== ========== ==========
       201 GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA
           ========== ========== ========== ========== ==========
       251 GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA
           ========== ========== ========== ========== ==========
       301 GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA GAGAGAGAGA
           ========== ========== ========== ========== ==========
       351 GAGAGAGAER ARGGSRERAR GRGRGRGEKR PRSPSSQSSS SGSPPRRPPP
           ========                                          ===
       401 GRRPFFHPVG EADYFEYHQE GGPDGEPDVP PGAIEQGPAD DPGEGPSTGP
           ====
       451 RGQGDGGRRK KGGWFGKHRG QGGSNPKFEN IAEGLRALLA RSHVERTTDE
       501 GTWVAGVFVY GGSKTSLYNL RRGTALAIPQ CRLTPLSRLP FGMAPGPGPQ
       551 PGPLRESIVC YFMVFLQTHI FAEVLKDAIK DLVMTKPAPT CNIRVTVCSF
       601 DDGVDLPPWF PPMVEGAAAE GDDGDDGDEG GDGDEGEEGQ E
HITS AT:   44-51, 91-358, 398-404

REFERENCE   1:  123:6883

L7   ANSWER 19 OF 24  REGISTRY  COPYRIGHT 2000 ACS
RN   161471-45-0  REGISTRY
CN   L-Arginine, L-arginyl-L-.alpha.-glutamyl-L-alanyl-L-valyl-L-
     alanylglycyl-L-arginylglycyl-L-arginylglycyl-L-arginylglycyl-L-
     arginylglycyl-L-arginylglycyl-L-arginylglycyl-L-arginylglycyl-L-
     arginylglycyl-L-arginylglycyl-L-arginylglycylglycyl-L-prolyl-L-
     arginyl- (9CI)  (CA INDEX NAME)
SQL  30

SEQ      1 REAVAGRGRG RGRGRGRGRG RGRGRGGPRR
                              = =======
HITS AT:   20-27

REFERENCE   1:  122:158385

L7   ANSWER 20 OF 24  REGISTRY  COPYRIGHT 2000 ACS
RN   155981-79-6  REGISTRY
CN   Antigen (human herpesvirus 4 58-amino acid fragment reduced) (9CI)
```

(CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Antigen (Epstein-Barr virus 58-amino acid fragment reduced)
OTHER NAMES:
CN Antigen (Epstein-Barr virus nuclear antigen-1 58-amino acid fragment)
CN Antigen (Epstein-Barr virus)
CI MAN
SQL 58

SEQ 1 PPRRPPPGRR PFFHPVGEAD YFEYHQECCD GEPDVPPGAI EQGPADDPGE
====== =
51 GPSTGPRG
HITS AT: 5-11

REFERENCE 1: 123:110142

REFERENCE 2: 121:33150

L7 ANSWER 21 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **155981-78-5** REGISTRY
CN Antigen (human herpesvirus 4 123-amino acid fragment) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Antigen (Epstein-Barr virus 123-amino acid fragment)
OTHER NAMES:
CN Antigen (Epstein-Barr virus nuclear antigen-1 123-amino acid fragment)
CN Antigen (Epstein-Barr virus)
CI MAN
SQL 123

SEQ 1 GGSGGRRGRG RERARGGSRE RARGRGRGRG EKRPRSPSSQ SSSSGSPPRR
51 PPPGRRPFFH PVGEADYFEY HQEGGPDGEP DVPPGAIEQG PADDPGEGPS
=======
101 TGPRGQGDGG RRKKGGWFGK HRG
HITS AT: 51-57

REFERENCE 1: 123:110142

REFERENCE 2: 121:33150

L7 ANSWER 22 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **155646-18-7** REGISTRY
CN Glycine, L-prolyl-L-arginyl-L-arginyl-L-prolyl-L-prolyl-L-prolylglycyl-L-arginyl-L-arginyl-L-prolyl-L-phenylalanyl-L-phenylalanyl-L-histidyl-L-prolyl-L-valylglycyl-L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-L-tyrosyl-L-phenylalanyl-L-.alpha.-glutamyl-L-tyrosyl-L-histidyl-L-glutaminyl-L-.alpha.-

glutamylglycylglycyl-L-prolyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Antigen (Epstein-Barr virus)
CI MAN
SQL 31

SEQ 1 PRRPPPGRRP FFHPVGEADY FEYHQEGGPD G
=======
HITS AT: 4-10

REFERENCE 1: 123:110142

REFERENCE 2: 121:33150

L7 ANSWER 23 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **139444-21-6** REGISTRY
CN L-Arginine, L-valyl-L-alanylglycyl-L-arginylglycyl-L-arginylglycyl-L-arginylglycyl-L-arginylglycyl-L-arginylglycyl-L-arginylglycyl-L-arginylglycyl-L-arginylglycylglycyl-L-prolyl-L-arginyl- (9CI) (CA INDEX NAME)
SQL 25

SEQ 1 VAGRGRGRGR GRGRGRGRGR GGPRR
====== ==
HITS AT: 15-22

REFERENCE 1: 120:214717

REFERENCE 2: 116:126815

L7 ANSWER 24 OF 24 REGISTRY COPYRIGHT 2000 ACS
RN **118440-43-0** REGISTRY
CN Antigen Sm-D (human clone D45-2 protein moiety) (9CI) (CA INDEX NAME)
CI MAN
SQL 119

SEQ 1 MKLVRFLMKL SHETVTIELK NGTQVHGTIT GVDVSMNTHL KAVKMTLKNR
51 EPVQLETLSI RGNRIRYFIL PDSLPLDTIR VDVEPKVKSK KREAVAGRGR
101 GRGRGRGRGR GRGRGGPRR
== ======
HITS AT: 109-116

REFERENCE 1: 110:52116

FILE 'CAPLUS' ENTERED AT 14:38:17 ON 06 DEC 2000
L8 139 SEA FILE=CAPLUS ABB=ON PLU=ON (EBV OR EB OR EPSTEIN BARR) AND (AUTOIMMUN? OR AUTO IMMUN?)(3A)(DISEAS? OR

-key terms

DISORDER)
L9 90 SEA FILE=CAPLUS ABB=ON PLU=ON L8 AND (ANTIBOD? OR (CELL OR CELLULAR)(3A)PROLIFERAT? OR MOLECUL? BIND? OR CYTOKINE OR (SKIN OR DERM?)(3A)(RXN OR REACT?) OR CELL SURFACE ANTIGEN)
L12 39 SEA FILE=CAPLUS ABB=ON PLU=ON L9 AND (DIAGNOS? OR DETERM? OR DETECT? OR DET## OR SCREEN? OR ASSAY?)

L13 37 L12 NOT L3

=> d 1-37 .beverly

L13 ANSWER 1 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:536175 CAPLUS
DOCUMENT NUMBER: 133:236509
TITLE: CD3.zeta. and CD28 down-modulation on CD8 T cells during viral infection
AUTHOR(S): Trimble, Linda A.; Kam, Lawrence W.; Friedman, Rachel S.; Xu, Zhan; Lieberman, Judy
CORPORATE SOURCE: Center for Blood Research, Harvard Medical School, Boston, MA, USA
SOURCE: Blood (2000), 96(3), 1021-1029
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Down-modulation of CD3.zeta. expression on CD8 T lymphocytes occurs, independently of other T-cell receptor (TCR)-CD3 components, in tumor-infiltrating lymphocytes, human immunodeficiency virus infection, and **autoimmune disease**. These assocns. suggest that it might be related to chronic antigenic stimulation. CD3.zeta. down-modulation was found, however, in CD8 T **cells** that **proliferate** in response to acute viral infections. In 3 otherwise healthy donors with acute gastroenteritis, infectious mononucleosis, and **Epstein-Barr** virus/cytomegalovirus/mononucleosis, 30% to 60% of circulating CD8 T cells had down-modulated CD3.zeta. to below the level of **detection**. The CD3.zeta.-T cells were also CD28- but expressed the activation markers HLA-DR and CD57. CD3.zeta.-CD28-T cells are effector CTL because they express perforin and produce IFN-.gamma., but not IL-2, on activation and contain the viral-specific cytotoxic T lymphocyte (CTL). However, CD3.zeta.-CD28-T cells generally do not express CD25 after anti-CD3 and anti-CD28 stimulation and are not cytotoxic until they are cultured with IL-2 overnight. Cytotoxicity coincides with the re-expression of CD3.zeta. but not CD28. Down-modulation of CD3.zeta. and CD28 on effector CTL may control CTL triggering and proliferation to prevent immunopathogenesis.
REFERENCE COUNT: 43

Searcher : Shears 308-4994

REFERENCE(S): (1) Altman, J; Science 1996, V274, P94 CAPLUS
(2) Azuma, M; J Immunol 1993, V150, P2091 CAPLUS
(3) Callan, M; J Exp Med 1998, V187, P1395 CAPLUS
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(6) Dutton, R; Annu Rev Immunol 1998, V16, P201 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:364744 CAPLUS
DOCUMENT NUMBER: 133:118844
TITLE: Glycine-rich cell wall proteins act as specific antigen targets in **autoimmune** and food allergic **disorders**
AUTHOR(S): Lunardi, Claudio; Nanni, Luca; Tiso, Micaela; Mingari, Maria Cristina; Bason, Caterina; Oliveri, Mara; Keller, Beat; Millo, Romano; De Sandre, Giorgio; Corrocher, Roberto; Puccetti, Antonio
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, University of Verona, Verona, 37134, Italy
SOURCE: Int. Immunol. (2000), 12(5), 647-657
CODEN: INIMEN; ISSN: 0953-8178
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Our objective was to investigate the presence of a B and T cell immune response directed against the glycine-rich cell wall protein (GRP) in patients with different **autoimmune disorders** and with food allergy. GRP is an ubiquitous food protein that has high homol. with cytokeratins and other self proteins [**Epstein-Barr** virus nuclear antigen-1 (EBNA-I), heterogeneous nuclear ribonucleoprotein, fibrillar collagen] which are common targets in **autoimmune disorders**. A peptide (GGYGDGGAHGGGYGG) derived from GRP was used to **screen** human sera in direct and competitive ELISA **assay**. Anti-GRP-specific IgG were analyzed for their ability to cross-react with autoantigens. The intracellular **cytokine** profiles of the peptide-specific T cell clones obtained from representative patients have been studied. BALB/c mice were immunized with the peptide coupled to the carrier protein keyhole limpet hemocyanin (KLH). Serum IgG **antibodies** directed against the GRP peptide were **detected** in several **autoimmune disorders** and in food allergic patients, and were able to cross-react with autoantigens including keratin, collagen and EBNA-I. Twenty-five T cell clones showed a specific proliferative response to the GRP peptide and were of the

Th0 phenotype. Eight of the 10 BALB/c mice immunized with the peptide coupled to KLH developed an autoimmune response. Our data suggest that phylogenetically highly conserved epitopes in plants, viruses and humans may be responsible for an autoimmune response in susceptible individuals. They also indicate that the antigen spreading of a particular sequence among apparently divergent proteins may participate to initiate or amplify an immune response.

REFERENCE COUNT: 43

REFERENCE(S):
(2) Atherton, E; Bioorg Chem 1979, V8, P351 CAPLUS
(4) Baboonian, C; Rheumatol Int 1989, V9, P161 CAPLUS
(6) Brunner, M; Eur J Immunol 1995, V25, P3285 CAPLUS
(7) Carter, L; Curr Opin Immunol 1997, V9, P177 CAPLUS
(8) Cortese, I; Proc Natl Acad Sci USA 1996, V93, P11063 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 2000:156805 CAPLUS

DOCUMENT NUMBER: 132:307151

TITLE: The Goodpasture autoantigen: Identification of multiple cryptic epitopes on the NC1 domain of the .alpha.3(IV) collagen chain

AUTHOR(S): Borza, Dorin-Bogdan; Netzer, Kai-Olaf; Leinonen, Anu; Todd, Parvin; Cervera, Javier; Saus, Juan; Hudson, Billy G.

CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, University of Kansas Medical Center, Kansas City, KS, 66160, USA

SOURCE: J. Biol. Chem. (2000), 275(8), 6030-6037
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Goodpasture (GP) **disease** is an **autoimmune disorder** in which autoantibodies against the .alpha.3(IV) chain of type IV collagen bind to the glomerular and alveolar basement membranes, causing progressive glomerulonephritis and pulmonary hemorrhage. Two major conformational epitope regions have been identified on the noncollagenous domain of type IV collagen (NC1 domain) of the .alpha.3(IV) chain as residues 17-31 (EA) and 127-141 (**EB**). To **det.** whether these regions are 2 distinct epitopes or form a single epitope, 3 GP sera were fractionated by affinity chromatog. on immobilized NC1 chimeras contg. the EA and/or the **EB** region. Four subpopulations

of GP **antibodies** with distinct epitope specificity for the .alpha.3(IV)NC1 domain were thus sepd. and characterized. They were designated GPA, GPB, GPAB, and GPX, to reflect their reactivity with EA only, **EB** only, both regions, and neither, resp. Hence, regions EA and **EB** encompass crit. amino acids that constitute 3 distinct epitopes for GPA, GPB, and GPAB **antibodies**, resp., whereas the epitope for GPX **antibodies** is located in a different unknown region. The GPA **antibodies** were consistently immunodominant, accounting for 60-65% of the total immunoreactivity to .alpha.3(IV)NC1; thus, they probably play a major role in pathogenesis. Regions EA and **EB** are held in close proximity because they jointly form the epitope for Mab3, a monoclonal **antibody** that competes for binding with GP autoantibodies. All GP epitopes are sequestered in the hexamer configuration of the NC1 domain found in tissues and are inaccessible for **antibody** binding unless dissocn. of the hexamer occurs, suggesting a possible mechanism for etiol. of GP disease. GP **antibodies** have the capacity to ext. .alpha.3(IV)NC1 monomers, but not dimers, from native human glomerular basement membrane hexamers, a property that may be of fundamental importance for the pathogenesis of the disease.

REFERENCE COUNT: 29

REFERENCE(S):
(1) Brainwood, D; Kidney Int 1998, V53, P762 CAPLUS
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(6) Gunwar, S; J Biol Chem 1998, V273, P8767 CAPLUS
(10) Hellmark, T; Kidney Int 1999, V55, P936 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 37 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 2000:139237 CAPLUS
DOCUMENT NUMBER: 133:188623

TITLE: Analysis of vH and vL genes of a monospecific human anti-myosin **antibody** produced by a B cell from the primary repertoire

AUTHOR(S): Laroche-Traineau, Jeanny; Biard-Piechaczyk, Martine; Jacobin, Marie-Josee; Chagnaud, Jean-Luc; Pau, Bernard; Nurden, Alan; Clofent-Sanchez, Gisele
CORPORATE SOURCE: CNRS UMR 5533, Hopital Cardiologique, Pessac, 33604, Fr.

SOURCE: Hum. Antibodies (1999), 9(3), 177-188
CODEN: HUANFP; ISSN: 1093-2607

Searcher : Shears 308-4994

PUBLISHER: IOS Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Epstein-Barr** virus (**EBV**) transformation of B lymphocytes from a Glanzmann's thrombasthenia patient with a serum **antibody** to the integrin .alpha.IIb.beta.3, led to the immortalization of a B cell secreting a monospecific IgM monoclonal **antibody** (MAb), B7, reactive with platelet myosin. Anal. of B7 V genes revealed minimally mutated sequences: the immortalized B cell issued from the primary repertoire, with no evidence of an in vivo selection by myosin. The V genes were here compared with sequences of human MAbs available on databases to more clearly understand the monospecificity of the B7 MAb. B7 V genes were closely identical to rearranged V genes in clones with self-specificities, often secreting polyreactive **antibodies**. In contrast, B7 is an unmutated monoreactive human MAb able to recognize myosin with a high avidity. Comparison of the CDR3H sequence with that of MAbs in databases supports a central role for the CDR3H subdomain in **detg**. monospecificity. Our results suggest the existence of a monospecific autoreactive B cell compartment, besides the well-known polyspecific one, susceptible to be the template of pathogenic autoreactivity, characterized by **antibodies** of high affinity and specificity.
REFERENCE COUNT: 56
REFERENCE(S): (4) Braun, J; J Clin Invest 1992, V89, P1395 CAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:795856 CAPLUS
DOCUMENT NUMBER: 132:34758
TITLE: Method for producing or enhancing a T-cell response against a target cell using a complex comprising an HLA class I molecule and an attaching means
INVENTOR(S): Savage, Philip Michael
PATENT ASSIGNEE(S): UK
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
Searcher : Shears 308-4994

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964464	A2	19991216	WO 1999-GB1764	19990604
WO 9964464	A3	20000203		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
GB 2339782	A1	20000209	GB 1999-8333	19990412
AU 9942767	A1	19991230	AU 1999-42767	19990604
PRIORITY APPLN. INFO.:			GB 1998-12227	19980605
			GB 1999-8333	19990412
			WO 1999-GB1764	19990604

AB A complex comprising an HLA class I mol. and attaching means for selectively attaching the HLA class I mol. to a target cell is disclosed, and a method is provided for producing or enhancing an immunol. response against a target cell, by attaching said complex to the target cell. Where the target cell is a diseased, foreign or malignant cell, this method may be used to promote the lysis of the target cell by T cells in the immune system. Where the target cell is an antigen presenting cell, this method may be used to promote the **proliferation** of specific T **cell** clones.
The invention is of potential use in the prevention and treatment of malignant diseases including cancer and leukemia, infectious diseases including viral infections such as HIV, bacterial infections including tuberculosis, and parasitic infections including malaria.

L13 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:793842 CAPLUS
DOCUMENT NUMBER: 132:136197
TITLE: Enhanced expression and autoimmunity of recombination signal binding protein-j.kappa. in human dilated cardiomyopathy
AUTHOR(S): Nickenig, Georg; Wolff, Marc; Stablein, Alexander; Pfister, Herbert; Bohm, Michael
CORPORATE SOURCE: Klinik III fur Innere Medizin, Universitat Koln, Koln, 50924, Germany
SOURCE: Biochem. Biophys. Res. Commun. (1999), 266(2), 432-436
CODEN: BBRCA9; ISSN: 0006-291X
Searcher : Shears 308-4994

PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dilated cardiomyopathy (DCM) is a major cause of heart failure in younger individuals. Its prognosis is poor with 40-50% of patients dying within 2 yr after **diagnosis**. Although the etiol. of DCM is poorly understood, there is increasing evidence that DCM may represent an **autoimmune disease** in a significant subset of patients. To identify candidate antigens in DCM, the authors applied a mol. strategy which combines recombinant expression cloning and autoimmunol. **screening** procedures. A left ventricle from a male DCM patient was explanted at heart transplantation and a human DCM left ventricular cDNA-expression library was constructed. 2.times.106 Clones were immunol. **screened** with serum collected from the same patient prior transplantation. Subsequent rounds of **screening** and purifn. allowed isolation of a pos. clone which was sequenced and identified as recombination signal binding protein-j.kappa. (RBP-j.kappa.). RBP-j.kappa. is an already identified transcription factor, e.g., involved in **Epstein-Barr** -virus-induced immortalization processes. Radioactively labeled RBP-j.kappa. protein was synthesized via in vitro translation using the isolated RBP-j.kappa. cDNA. This RBP-j.kappa. protein was used for immunopptn. reactions to **screen** sera of healthy controls and patients suffering of DCM for the presence of RBP-j.kappa. autoantibodies. Anal. revealed that only 31% of healthy but 70.6% of DCM patients carry an autoantibody against RBP-j.kappa.. Patients suffering from ischemic cardiomyopathy showed a prevalence of 22% of RBP-j.kappa. autoantibodies. Western anal. with an monoclonal **antibody** raised against RBP-j.kappa. showed that RBP-j.kappa. was overexpressed to 488% in DCM hearts compared to non-failing controls. Autologous immunol. **screening** of a cDNA expression library is a powerful and novel technol. to gain insights into the etiol. of human idiopathic DCM. Human DCM displays an autoimmune response against RBP-j.kappa. and an overexpression of RBP-j.kappa.. Since RBP-j.kappa. is involved in cellular immortalization and exerts anti-apoptotic effects, the increased RBP-j.kappa. autoantibody level during DCM may inhibit this growth-regulating feature of RBP-j.kappa.. In this setting, enhanced myocardial RBP-j.kappa. expression could represent a compensatory but ineffective response to counteract the increased rate of apoptosis in DCM. Furthermore, RBP-j.kappa. may be a useful **diagnostic** marker for DCM. (c) 1999 Academic Press.

REFERENCE COUNT: 26
REFERENCE(S):
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(8) Kandolf, R; Proc Natl Acad Sci 1987, V84, P6272 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:199556 CAPLUS
DOCUMENT NUMBER: 130:280837
TITLE: T cell clone for **screening** disease-treating agent
INVENTOR(S): Matsui, Takashi; Kaneko, Fumio
PATENT ASSIGNEE(S): Hitachi Chemical Co., Ltd., Japan; Kaneko, Fumio
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11075890	A2	19990323	JP 1997-234298	19970829

AB Disclosed is a method for T cell cloning from patient using B cell-based feeder cell coculture system. The feeder cell may be **Epstein-Barr** virus-transformed and mitomycin-treated B cells. The patient-derived T cell clone is prepd. for evaluation and **screen** of therapeutic (for allergy, atopic dermatitis, **autoimmune disease**, T cell lymphoma, etc.) with reduced risk for being infected by T cell-infective virus. Thus, peripheral blood was obtained from patients with atopic dermatitis, T lymphocytes were isolated, isolated T cells were cultured in the supernatant of **Epstein -Barr** virus-transformed B958 cells, and the produced T cell clone was characterized for **cytokine** prodn. (i.e. interferon .gamma., interleukin 4, and helper T cell subclass) and used for evaluation of effectiveness of dexamethasone for treating atopic dermatitis.

L13 ANSWER 8 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:391389 CAPLUS
DOCUMENT NUMBER: 129:159957
TITLE: **Determination** of **Epstein-Barr** virus association with B-cell lymphomas in Japan: study of 72 cases-in situ hybridization, polymerase chain reaction, immunohistochemical studies
AUTHOR(S): Hirose, Yuko; Masaki, Yasufumi; Sasaki, Keiko; Ogawa, Yoshimi; Takeshita, Shoichi; Fukutoku, Masaaki; Sugai, Susumu; Takiguchi, Tomoo

CORPORATE SOURCE: Division of Hematology and Immunology, Department of Internal Medicine, Kanazawa Medical University, Uchinada, 920-02, Japan
SOURCE: Int. J. Hematol. (1998), 67(2), 165-174
CODEN: IJHEEY; ISSN: 0925-5710
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The assocn. of **Epstein-Barr** virus (**EBV**) with B-cell lymphoma was examd. in 72 human immunodeficiency virus-neg. Japanese patients using the polymerase chain reaction (PCR) on DNA obtained from formalin-fixed paraffin-embedded tissues and an in situ hybridization (ISH) technique. **EBV**-encoded RNA 1 (EBER-1) was **detected** in 12 of 72 cases (17%); five of 33 cases (15%) of nodal B-cell lymphomas and seven of 39 cases (18%) of extranodal B-cell lymphomas. Three cases of post-bone marrow transplantation and one case of **autoimmune disease** (Evans syndrome) were included among seven EBER-1 pos. extranodal lymphomas. A combined study of immunohistochem. and EBER-1 revealed that some L26 pos. cells were EBER-1 pos. A DNA band was also obsd. in 13 of 70 examd. cases (19%) (four of 33 cases of nodal B-cell lymphomas (12%) and nine of 37 cases of extranodal B-lymphomas (24%)) in the PCR study using primers to **detect** the Barn HI-W fragment of **EBV**. In the immunohistochem. study using a monoclonal **antibody** to the latent membrane protein 1 (LMP-1) of the **EBV**, one of the **EBV**-encoded latent gene products, LMP-1, was expressed in six of 34 cases (18%) of extranodal B-lymphomas, but none of the cases with nodal B-cell lymphomas were shown to be LMP-1 pos. Oncoprotein bcl-2 was examd. by immunohistochem. and expressed in seven cases of nodal lymphomas and three cases of extranodal lymphomas, and two of these nodal cases were EBER ISH pos. In **EBV** serol., only two cases of nodal and one case of extranodal EBER pos. B-cell lymphomas revealed a reactivation pattern. In the PCR study using primers to **detect** the lymphocyte-**detd**. membrane antigen (LYDMA), the same sized monoclonal bands were obsd. in case 36 in the PCR products from the nose and skin, suggesting the monoclonal proliferation of the tumor. These findings suggested a low incidence of **EBV** assocn. with B-cell lymphomas unless patients were in an immunol. impaired condition such as post-organ transplantation or **autoimmune diseases**.

L13 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:195147 CAPLUS
DOCUMENT NUMBER: 128:320488
TITLE: Chronic parvovirus B19 infection induces the production of anti-virus **antibodies** with autoantigen binding properties
AUTHOR(S): Lunardi, Claudio; Tiso, Micaela; Borgato,

Lorena; Nanni, Luca; Millo, Romano; De Sandre, Giorgio; Bargellesi Severi, Antonio; Puccetti, Antonio
CORPORATE SOURCE: Institute Clinica Medica, University Verona, Verona, Italy
SOURCE: Eur. J. Immunol. (1998), 28(3), 936-948
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human parvovirus B19 infection in adults shows some clin. features similar to those found in **autoimmune** connective tissue **diseases**. To better clarify the relation between viral infection and autoimmunity, the authors have evaluated the ability of anti-parvovirus **antibodies** to specifically recognize autoantigens in patients with chronic sym. arthritis resembling rheumatoid arthritis or with recurrent episodes of arthritis and cutaneous manifestations and persistence of specific IgM **antibodies** against B19 parvovirus. A 24-amino acid immunodominant peptide was synthesized corresponding to a part of the virus protein 1 and virus protein 2 overlapping region. The peptide was used to test patients' sera at different time points with an ELISA and to purify anti-virus **antibodies** by affinity chromatog. on a peptide-Sepharose column. Eluted Igs recognized the B19 peptide in both direct and competitive ELISA. Affinity-purified anti-parvovirus **antibodies** were then tested on a panel of autoantigens including human keratin, collagen type II, thyroglobulin, single-strand (ss)DNA, cardiolipin, and ribonucleoprotein antigen Sm. Eluted **antibodies** specifically recognized keratin, collagen type II, ssDNA, and cardiolipin. Autoantibody activity was not **detected** in the Ig fraction after complete removal of anti-peptide **antibodies** and in **antibodies** eluted from normal donors. **Epstein-Barr** virus-transformed cell clones obtained from 2 subjects produced **antibodies** which simultaneously recognize the viral peptide and several autoantigens. To further confirm the role of the virus in inducing an autoantibody response, 8 BALB/c mice were immunized with the viral peptide coupled to a carrier protein. Autoantibody activity against keratin, collagen II, cardiolipin, and ssDNA was **detected** in 6 of the 8 mice which developed a strong anti-virus response. These data indicate that B19 parvovirus may be linked to the induction of an autoimmune response.

L13 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:163620 CAPLUS
DOCUMENT NUMBER: 128:229362
TITLE: Novel combination preparations and their use in immunodiagnosis and immunotherapy

INVENTOR(S): Bohlen, Heribert
PATENT ASSIGNEE(S): Viva Diagnostika Diagnostische Produkte G.m.b.H., Germany; Bohlen, Heribert
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808875	A1	19980305	WO 1997-EP4493	19970818
W: AU, BR, BY, CA, CN, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SI, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19634730	A1	19980305	DE 1996-19634730	19960828
DE 19703699	A1	19980806	DE 1997-19703699	19970203
AU 9741193	A1	19980319	AU 1997-41193	19970818
PRIORITY APPLN. INFO.:			DE 1996-19634730	19960828
			DE 1997-19703699	19970203
			WO 1997-EP4493	19970818

AB Combination prepns. comprising 3 components are provided for specific purposes in immunol., **diagnosis**, and therapy. The combination is based on the universal use of an immunolinker which can link .gtoreq.2 other different components provided with different **determinants**. The immunolinker may be an inert particle bearing reagents specific for .gtoreq.2 **determinants**, a bispecific **antibody**, a protein, etc. One of the other components is a target-specific immunol. reagent bearing an antigenic **determinant**, e.g. a hapten, epitope, paratope, or idiotope specific for 1 of the linker reagents as well as a target-specific reagent (protein, Ig, **antibody** , **antibody** fragment, ligand, lectin, receptor-binding mol., adhesion mol., **cytokine**, etc.). The 3rd component is a biol. active or **detectable** substance (enzyme, radiolabel, contrast agent, cytostatic agent, prodrug, adhesion mol., **cytokine**, ligand, **antibody**, etc.) bearing a **determinant** specific for the other reagent on the linker. Thus, mice were immunized with both 2,4-dinitrophenol (DNP) and digoxigenin, and myeloma cells and spleen cells from the immunized mice were fused by the PEG method to provide hybridoma cells which were selected for prodn. of monoclonal **antibodies** to DNP or digoxigenin. Cells from the 2 hybridoma lines were then fused and selected for prodn. of bispecific **antibodies** to DNP and digoxigenin. The bispecific **antibody** was used in combination with a DNP-labeled OKT (anti-CD3) monoclonal **antibody** and a

digoxigenin-labeled anti-CD19 monoclonal **antibody** for incubation with cytotoxic T-cells and Eu-labeled **Epstein-Barr** virus-immortalized B-cells in a cytotoxic FIA.

L13 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:351124 CAPLUS
DOCUMENT NUMBER: 126:316338
TITLE: A heterodimer of **Epstein-Barr** virus induced protein 3 and interleukin 12 p35 subunit as a novel hematopoietic **cytokine** and uses therefor
INVENTOR(S): Devergne, Odile; Kieff, Elliott D.
PATENT ASSIGNEE(S): Brigham and Women's Hospital, Inc., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9713859	A1	19970417	WO 1996-US16572	19961011
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5830451	A	19981103	US 1996-684687	19960719
PRIORITY APPLN. INFO.:			US 1995-5092	19951011
			US 1996-684687	19960719

AB A novel heterodimeric hematopoietic **cytokine** formed from the **Epstein Barr** virus-induced protein 3 (EBI3) and the p35 subunit of interleukin-12 (IL12) is described. **Antibodies** to the heterodimer are prepd. and cDNAs encoding the subunits are cloned and expressed. The **cytokine** is of therapeutic use, including **diagnostic assays** for **detecting** pregnancy or threatened spontaneous abortion using **antibodies** to the **cytokine**.

L13 ANSWER 12 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:185018 CAPLUS
DOCUMENT NUMBER: 126:292275
TITLE: Identification, expression, and immunogenicity of Kaposi's sarcoma-associated herpesvirus-encoded small viral capsid antigen
AUTHOR(S): Lin, Su-Fang; Sun, Ren; Heston, Lee; Gradoville, Lyn; Shedd, Duane; Haglund, Karl; Rigsby, Michael; Miller, George
CORPORATE SOURCE: Dep. Mol. Biophys. & Biochem., Yale Univ. Sch. Med., New Haven, CT, 06520, USA
Searcher : Shears 308-4994

SOURCE: J. Virol. (1997), 71(4), 3069-3076
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors describe a recombinant antigen for use in serol. tests for **antibodies** to Kaposi's sarcoma (KS)-assocd. herpesvirus (KSHV). The cDNA for a small viral capsid antigen (sVCA) was identified by immunoscreening of a library prepd. from the BC-1 body cavity lymphoma cell line induced into KSHV lytic gene expression by sodium butyrate. The cDNA specified a 170-amino-acid peptide with homol. to small viral capsid proteins encoded by the BFRF3 gene of **Epstein-Barr** virus and the ORF65 gene of herpesvirus saimiri. KSHV sVCA was expressed from a 0.85-kb mRNA present late in lytic KSHV replication in BC-1 cells. This transcript was sensitive to phosphonoacetic acid and phosphonoformic acid, inhibitors of herpesvirus DNA replication. KSHV sVCA expressed in mammalian cells or Escherichia coli or translated in vitro was recognized as an antigen by antisera from KS patients. Rabbit antisera raised to KSHV sVCA expressed in E. coli **detected** a 22-kDa protein in KSHV-infected human B cells. Overexpressed KSHV sVCA purified from E. coli and used as an antigen in immunoblot **screening assay** did not cross-react with **EBV** BFRF3. **Antibodies** to sVCA were present in 89% of 47 human immunodeficiency virus (HIV)-pos. patients with KS, in 20% of 54 HIV-pos. patients without KS, but in none of 122 other patients including children born to HIV-serpos. mothers and patients with hemophilia, **autoimmune disease**, or nasopharyngeal carcinoma. Low-titer **antibody** was **detected** in three sera from 28 healthy subjects. **Antibodies** to recombinant sVCA correlate with KS in high-risk populations. Recombinant sVCA can be used to exam. the seroepidemiol. of infection with KSHV in the general population.

L13 ANSWER 13 OF 37 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1996:649425 CAPLUS
DOCUMENT NUMBER: 125:326250

TITLE: Comparison of rheumatoid factors of rheumatoid arthritis patients, of individuals with mycobacterial infections and of normal controls. Evidence for maturation in the absence of an autoimmune response

AUTHOR(S): Djavad, Nargues; Bas, Sylvette; Shi, Xiaowen; Schwager, Joseph; Jeannet, Michel; Vischer, Thomas; Roosnek, Eddy
CORPORATE SOURCE: Department Medicine, Universitaire Geneve, Geneva, CH-1211, Switz.

SOURCE: Eur. J. Immunol. (1996), 26(10), 2480-2486

CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The rheumatoid factors (RF) was analyzed produced by **Epstein -Barr** virus-transformed monoclonal B cells established from patients with rheumatoid arthritis (RA), and individuals with a history of Mycobacterium tuberculosis (TB). Fifty-eight RF were analyzed for specific activity (IU-RF/.mu.g) for the Fc part of IgG and their interaction with tetanus toxoid (TT) and DNA (polyspecificity). The V-D-J heavy chain region of 16 (9TB-/7RA-) RF was sequenced. Differences were obsd. between the NI-RF and the TB- and RA-RF. While the RF repertoire of normal individuals comprised of low-avidity RF of which the majority (15/17) were polyspecific, more than half of the TB- and RA-RF were monoreactive. The monospecific TB- and RA-RF were of higher avidity than the NI-RF (RA > TB > NI). With respect to polyspecificity, the RF in the groups were comparable: the interaction with DNA, TT as well as with Fc was inhibited either by an increase of the ionic strength to 0.3-0.5 M NaCl or by addn. of the polyanion dextran sulfate, indicating that the **antibodies** interacted with similar anionic epitopes shared by the 3 antigens. Anal. of the V-D-J heavy chain regions showed differences between the resp. RF. The salt-sensitive binding was highly correlated with the presence of arginine in the complementarity-**detg**. region 3 (CDR3). Whereas the polyspecific RF consisted predominantly of germ-line encoded **antibodies**, the genes of the monospecific RA/TB-RF were somatically mutated (RA > TB). It is therefore likely that maturation of RF can be initiated by chronic infections and that monospecific, somatically mutated RF are not a unique characteristic of **autoimmune diseases**.

L13 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:581608 CAPLUS
DOCUMENT NUMBER: 125:273143
TITLE: Molecular analysis of stimulatory anti-thyrotropin receptor **antibodies** (TSAbs) involved in Graves' disease: isolation and reconstruction of **antibody** genes, and production of monoclonal TSAbs
AUTHOR(S): Akamizu, Takashi; Matsuda, Fumihiko; Okuda, Jyoji; Li, Hua; Kanada, Hidetoshi; Watanabe, Takeshi; Honjo, Tasuku; Mori, Toru
CORPORATE SOURCE: Dep. of Laboratory Medicine, Kyoto University, Kyoto, Japan
SOURCE: J. Immunol. (1996), 157(7), 3148-3152
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Anti-TSH receptor autoantibodies (TRAbs) have been known to be

involved in Graves' disease. To understand the mol. mechanism for pathogenesis of TSAbs in Graves' disease, we isolated and reconstituted the Ig genes of **EBV**-transformed B cell clones producing monoclonal thyroid stimulating Ab (TSAb) obtained from patients with Graves' disease. The V region genes of Ig heavy (H) and light (L) chains of two TSAb clones, IgG clone B6B7 and IgM clone 101-2, were isolated by the PCR. Nucleotide sequencing anal. revealed that germ-line VH and V.kappa. segments widely used for autoantibodies including the previously isolated TRAbs were utilized in the two clones. A significant no. of somatic mutations were found in V regions of both clones, indicating the involvement of somatic mutations for the TSAb specificity. Reconstituted IgH and L chain genes of the two clones were stably introduced into myeloma cells for IgG1 prodn. IgGs purified from cultured supernatants of both transfectants exhibited significant TSAb activities, while they did not inhibit TSH binding to the receptor. The successful expression of recombinant TSAbs in eukaryotic cells will provide opportunities to apply them to various pathophysiol., **diagnostic** and therapeutic investigations in **autoimmune** thyroid **diseases**.

L13 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:567823 CAPLUS
DOCUMENT NUMBER: 125:219432
TITLE: Human immunoglobulin G autoantibodies to the thyrotropin receptor from **Epstein-Barr** virus-transformed B lymphocytes: characterization by immunoprecipitation with recombinant antigen and biological activity
AUTHOR(S): Morgenthaler, Nils G.; Kim, Mi Rim; Tremble, Jennifer; Huang, Guo Cai; Richter, Wiltrud; Gupta, Manjula; Scherbaum, Werner A.; McGregor, Alan M.; Banga, J. Paul
CORPORATE SOURCE: Department Medicine, King's College School Medicine, London, SE5 9PJ, UK
SOURCE: J. Clin. Endocrinol. Metab. (1996), 81(9), 3155-3161
CODEN: JCEMAZ; ISSN: 0021-972X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The TSH receptor (TSH-R) is the target antigen for disease-related autoantibodies in Graves' disease and primary myxoedema, but the repertoire of the **antibodies** or the nature of the precise antigenic epitopes is not known. The authors have immortalized peripheral blood B cells from 6 different **autoimmune** thyroid **disease** patients with **Epstein-Barr** virus and selected IgG-producing B cells by magnetic selection on anti-IgG-coated beads. Purified recombinant insect cell-derived extracellular region of TSH-R was used to identify the

pos. wells for expansion in culture. Stable B cell lines were obtained, which after limiting diln. led to two stable B cell clones. B cell lines and clones secreted IgG **antibody** that were shown to react biochem. with metabolically labeled or in vitro translated, nascent extracellular region of TSH-R, giving strong confirmatory evidence of the presence of anti-TSH-R **antibody**. Supernatants from lines contained thyroid-stimulating activity, thyroid-blocking activity (as assessed by inhibition of TSH-mediated cAMP stimulation), or both of these activities. Interestingly, **antibodies** with stimulating activity were generated from a primary myxoedema patient, and **antibodies** of blocking specificities were obtained from newly **diagnosed** thyrotoxic Graves' disease patients. The results favor a fine balance between stimulating and blocking autoantibody activities in **detg**. the clin. presentation obsd. in patients with **autoimmune** thyroid **disease** patients who have these **antibodies** present in their serum.

L13 ANSWER 16 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:487469 CAPLUS
DOCUMENT NUMBER: 125:140384
TITLE: Generation and characterization of a human monoclonal autoantibody that acts as a high affinity interleukin-1.alpha. specific inhibitor
AUTHOR(S): Garrone, Pierre; Djossou, Odile; Fossiez, Francois; Reyes, Jean; Ait-Yahia, Smina; Maat, Corien; Ho, Stephen; Hauser, Thomas; Dayer, Jean-Michel; et al.
CORPORATE SOURCE: Schering-Plough, Lab. Immunol. Res., Dardilly, 69571, Fr.
SOURCE: Mol. Immunol. (1996), 33(7/8), 649-658
CODEN: MOIMD5; ISSN: 0161-5890
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Interleukin-1 (IL-1) defines two polypeptides, IL-1.alpha. and IL-1.beta., that possess a wide spectrum of biol. effects. Two natural antagonists of IL-1 action have been characterized: the IL-1 receptor antagonist (IL-1Ra) and a sol. form of the type II IL-1 receptor. Neutralizing autoantibodies to IL-1.alpha. have also been **detected** in sera of healthy individuals and patients with **autoimmune** or inflammatory **diseases**. To characterize such **antibodies** molecularly, we attempted to generate B cell clones producing anti-IL-1.alpha. human monoclonal **antibody** (HuMAb) by combining **Epstein-Barr** virus-immortalization and CD40-activation of B lymphocytes from individuals with circulating anti-IL-1.alpha.. We describe herein the generation and properties of a natural IgG4/.kappa. anti-IL-1.alpha. monoclonal autoantibody, HuMAb X3, that bound specifically to human IL-1.alpha., but not to IL-1.beta. and IL-1Ra,

with a high affinity (Kd = 1.2 .times. 10-10 M). HuMAb X3 inhibited IL-1.alpha. binding to IL-1 receptors and neutralized biol. activities of both recombinant and natural forms of IL-1.alpha.. A recombinant form of HuMAb X3 was found to display identical specific IL-1.alpha. antagonism. The presence of somatic mutations within X3 variable regions suggests an antigen-driven affinity maturation. This study extends the demonstration of the presence of high affinity neutralizing anti-IL-1.alpha. autoantibodies that can function as a third type of IL-1 antagonist.

L13 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:999540 CAPLUS
DOCUMENT NUMBER: 124:30438
TITLE: Preparation of oligopeptide having binding affinity to HLA human histocompatibility antigen HLA-DRB1*0405
INVENTOR(S): Matsushita, Sho; Nishimura, Taiji; Takahashi, Katsushi; Komorya, Keiji
PATENT ASSIGNEE(S): Teijin Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07206896	A2	19950808	JP 1994-4615	19940120

OTHER SOURCE(S): MARPAT 124:30438
AB Oligopeptides contg. an amino acid sequence X1-Y1-Y2-X2-Y3-X3 (I; X1 = amino acid selected from W, F, L, M, Y, and I; X2 = amino acid selected from F, L, I, Y, W, C, V, M, and A; X3 = amino acid selected from N, D, T, I, V, S, F, M, and W; Y1, Y2 = any L-amino acid), preferably I (X1 = W and X2 = L; X1 = F and X2 = L; X1 = X2 = F; X1 = M and X2 = L; X1 = F and X2 = I; X3 = N), are prepd. as immunosuppressants. Seven oligopeptides, e.g. GSTVFDNLPNPEIDGDYYGW (II), were isolated by culturing **Epstein-Barr** virus-infected lymphocytes of a patient having HLA-DRB1*0405 antigen and purifn. using anti-DR **antibody**-immobilized column. Based on the sequence of these natural oligopeptides and sequence homol. search on known proteins, 7 oligopeptides contg. each of the above 7 oligopeptide sequences, i.e. II, VPIQRAVYQNVVVNN (III), SPGTGAYYVLLN (IV), EGQLVSIHSPEEQDFLTKHA (V), GPKPLFRRMSSLVGPTQSFF (VI), GKPPQYIAVHVVPDQLMAFG (VII), SDPILYRPVAVALDTKGPE (VIII), were postulated to be HLA-DRB1*0405 binding oligopeptides and were synthesized by a peptide synthesizer and **assayed** for the binding affinity to HLA-DRB1*0405 antigen. For example, the binding ratio of [125I]II to HLA-DRB1*0405 antigen was 12.7%, which was

highest among these 7 oligopeptides. A series of fifteen analogs of I, which were GSTVFDNLPNPE (IX) and its analogs with either one hydrophilic amino acid replaced by alanine or one hydrophobic amino acid replaced by serine, e.g. GSTVSDNLPNPE (X), were also prepd. and **assayed** for inhibiting the binding of [125I]II to HLA-DRB1*0405 antigen. IX and X showed 100 and 0% inhibition, resp., and this **assay** revealed that the following amino acid sequence motif (----F--L-N--; wherein - indicates the other amino acids in the peptide) in I were important for strong binding inhibition. After similarly examg. other 6 oligopeptides III - VIII, the amino acid sequence motifs (--Y--L-N--, --Y--V-V--, --L--I-S--, and --F--M-S--) were also found to be essential for potent binding inhibition. These amino acid sequence motifs provide important information for identification of autoantigens in **autoimmune diseases** such as chronic arthrorheumatism and peptides contg. these motifs are useful as immunosuppressants.

L13 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:939214 CAPLUS
DOCUMENT NUMBER: 124:27441
TITLE: Interleukin-12
AUTHOR(S): Germann, Tieno; Rnede, Erwin
CORPORATE SOURCE: Institute Immunology, Mainz, Germany
SOURCE: Int. Arch. Allergy Immunol. (1995), 108(2), 103-12
CODEN: IAAIEG; ISSN: 1018-2438
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 120 refs. Interleukin (IL)-12 was originally identified as a factor produced by human **Epstein-Barr** virus-transformed B cell lines. It was **detected** by one group as cytotoxic lymphocyte maturation factor, a **cytokine** that synergized with IL-2 in the induction of lymphokine-activated killer cells and cytotoxic T lymphocytes. A second group characterized it as a natural killer (NK) cell stimulatory factor, due to the enhancement of cytotoxicity and IFN-.gamma. synthesis by NK cells. Human IL-12 was purified to homogeneity and cloned by both groups. The authors had identified a murine factor, provisionally termed T cell-stimulating factor (TSF), which was involved in the proliferation, synthesis of IFN-.gamma. and cell adhesion of CD4+ Th1 cells. TSF was produced in the antigen-specific interaction between Th1 cells and macrophages as antigen-presenting cells, partially purified from supernatants of such cultures, and shown to be identical to IL-12. Monocytes/macrophages appear to be the major source of IL-12. It is rapidly produced by phagocytic cells after stimulation with several bacteria/bacterial products and other microorganisms. In the light of its effects on NK cells as well as CD4+ and CD8+ T cells, IL-12

can be regarded as a **cytokine** that connects the innate immune system with the acquired immunity. IL-12 has a broad range of activities already reviewed in three papers. These include the regulation of **cytokine** synthesis and proliferation of T and NK cells, the promotion of Th1 cell development, the differentiation of CD8+ T cells and effects on hematopoiesis. When applied in vivo, IL-12 was shown to enhance the resistance to bacterial and parasitic infections, to promote antitumor immunity, and to influence antiviral responses including HIV in vivo or in vitro. This review will briefly summarize these effects, but mainly focus on recent results concerning the regulation of the prodn. and the activity of IL-12, its role in the differentiation of Th cells and the implications for delayed and immediate-type hypersensitivity reactions, its importance for organ-specific **autoimmune diseases**, and the possible role of the IL-12p40 homodimer as a specific inhibitor of the IL-12 heterodimer.

L13 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:865706 CAPLUS
DOCUMENT NUMBER: 123:311954
TITLE: In vitro production of human anti-sperm **antibodies** and the effect of an oligoclonal **antibody** (F6) on sperm-egg interaction
AUTHOR(S): Fusi, F. M.; Besuschio, F.; Santis, L. De; Lorenzetti, I.; Ferrari, A.
CORPORATE SOURCE: Istituto Scientifico San Raffaele, University Milan, Milan, Italy
SOURCE: J. Reprod. Immunol. (1995), 29(2), 135-47
CODEN: JRIMDR; ISSN: 0165-0378
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A method has been developed to establish lines of transformed lymphocytes able to produce in vitro the same anti-sperm **antibodies** as those naturally occurring in immuno-infertile individuals. We utilized lymphocytes from a male donor whose serum contained anti-sperm **antibodies** of the IgG class up to the diln. 1:10 000, as **detected** by means of immunobead binding. T lymphocytes were sepd. from B lymphocytes using magnetic beads coated with anti-T **antibody**. B lymphocytes were then placed at a concn. of 5 .times. 106/mL in a 96-well plate, stimulated with phytohemagglutinin (PHA) and transformed with **Epstein-Barr** virus. After a few days, only transformed cells continued growing and these were collected. The supernatant was tested for prodn. of anti-sperm **antibodies** and those transformed lymphocytes shown to be synthesizing **antibodies** directed against the sperm head and the tail were cloned. We obtained a clone of cells producing **antibodies** of the IgG1 class directed against the head of the spermatozoon.

This oligoclonal **antibody** (F6) recognized a 58-kDa band from a lysate of sperm membranes and was able to reduce the penetration of zona-free hamster oocytes by capacitated spermatozoa.

L13 ANSWER 20 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:558387 CAPLUS
DOCUMENT NUMBER: 123:31066
TITLE: **Detection** of **Epstein-Barr** virus and cytomegalovirus genome in white blood cells from patients with juvenile rheumatoid arthritis and childhood systemic lupus erythematosus
AUTHOR(S): Tsai, Yann-Tourn; Chiang, Bor-Luen; Kao, Yun-Feng; Hsieh, Kue-Hsiung
CORPORATE SOURCE: College of Medicine, National Taiwan University, Taipei, Peop. Rep. China
SOURCE: Int. Arch. Allergy Immunol. (1995), 106(3), 235-40
CODEN: IAAIEG; ISSN: 1018-2438
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of infectious agents in the pathogenesis of **autoimmune diseases** has long been a matter of debate. This study investigated the possible role of **Epstein-Barr** virus (**EBV**) and human cytomegalovirus (HCMV) infections in the pathogenesis of **autoimmune diseases** by an attempt to demonstrate the presence of the viral genome in the leukocyte of 21 juvenile rheumatoid arthritis (JRA) patients, 20 childhood-onset systemic lupus erythematosus (SLE) patients, and 20 age matched normals, using polymerase chain reaction (PCR) and DNA probes. The results showed: (1) there was no difference in serum IgG anti-**EBV** **antibody** titers among three groups; (2) the **EBV** PCR-pos. rates for JRA and SLE patients and normal controls were 5% (1/21), 10 (2/20), and 0% (0/20), resp.; (3) the HCMV PCR-pos. rates for JRA and SLE patients and normal controls were 33% (7/21), 25 (5/20), and 10% (2/20), resp., and (4) the HCMV-pos. rate was 25% for JRA patients with steroid treatment and 33% for those without steroid treatment. It is, therefore, concluded that: (1) the data do not support the participation of **EBV** and HCMV in the pathogenesis of childhood-onset SLE and JRA; (2) steroid therapy does not increase the frequency of HCMV infection in JRA patients, and (3) immunoincompetence might be one of the major factors contributing to increased susceptibility to HCMV infection in JRA and SLE patients.

L13 ANSWER 21 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:436297 CAPLUS
DOCUMENT NUMBER: 122:211944

TITLE: **Epstein-Barr** virus-induced autoimmune responses. II. Immunoglobulin G autoantibodies to mimicking and nonmimicking epitopes. Presence in **autoimmune disease**

AUTHOR(S): Vaughan, John H.; Nguyen, Minh-Duc; Valbracht, Jean R.; Patrick, Kevin; Rhodes, Gary H.

CORPORATE SOURCE: Dep. Medicine, Univ. Calif., San Diego, La Jolla, CA, 92093-0663, USA

SOURCE: J. Clin. Invest. (1995), 95(3), 1316-27
CODEN: JCINAO; ISSN: 0021-9738

DOCUMENT TYPE: Journal

LANGUAGE: English

AB During infectious mononucleosis, IgM autoantibodies are generated to a protein, p542, which contains a glycine-rich 28-mer epitope cross-reactive with the **Epstein-Barr** nuclear antigen-1 through **Epstein-Barr** nuclear antigen-1's glycine/alanine repeat. In normal individuals it is uncommon to find IgG anti-p542, but among patients with progressive systemic sclerosis, systemic lupus erythematosus, and ulcerative colitis high IgG anti-p542 (>3 SD above the mean of normal 20-50 yr controls) occurred frequently. Lesser elevations occurred in Sjogren's syndrome, rheumatoid arthritis, ankylosing spondylitis, and Crohn's disease, but none with chronic hepatitis B infection. The reactive epitopes on p542 were mapped with deletion mutants, which indicated that the glycine-rich 28-mer was the major antigenic **determinant**, with lesser **antibody** responses to other epitopes. We conclude that normally there is an inability to generate IgG autoantibodies to the cross-reactive (mimicking) epitope of the p542 host protein, but that this inability is overcome in a proportion of patients with **autoimmune disease**. We conclude also that non-cross-reactive autoepitopes exist on p542 protein, to which IgG autoantibodies can commonly be formed in **autoimmune disorders**. The mechanisms responsible for the latter must involve different mechanisms than those responsible for autoantibodies to the mimicking epitope.

L13 ANSWER 22 OF 37 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1994:104290 CAPLUS

DOCUMENT NUMBER: 120:104290

TITLE: Investigation of agretopic motifs in T cell responses specific for pigeon cytochrome c related peptides and restricted to I-E molecules

AUTHOR(S): Gotohda, Toshihiko

CORPORATE SOURCE: Inst. Immunol. Sci., Hokkaido Univ., Sapporo, 060, Japan

SOURCE: Hokkaido Igaku Zasshi (1993), 68(6), 801-12
CODEN: HOIZAK; ISSN: 0367-6102

DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB In the authors' previous study, epitopic and agretopic residues of a peptide fragment deduced from pigeon cytochrome c43-58 (p43-58, AEGFSYTDANKNKGIT) and it's analogs in the T cell responses restricted to I-A mols. were **detd**. It has been shown that amino acid residue position 50 of the p43-58 works as an epitope which contacts with T cell antigen receptor (TCR) and residues at positions 46 and 54 function as agretopes which contact with I-A mols. In the present study, epitopic and agretopic sites were analyzed in T **cell proliferative** responses that were restricted to the other class II antigen, I-E, mols. A peptide antigen, 46D50V54R, which had been prepd. by substitution of amino acids at positions 46, 50, and 54 of p43-58 with aspartic acid (D), valine (V), and arginine (R), resp., was shown to induce class II restricted T cell responses in B10.A(3R)(I-Ab, I-**Eb**/k) but not in B10 (I-Ab, I-E-) mice. Similarly, 50V54R which had been prepd. by substitution of amino acids at positions 50 and 54 with V and R, resp. induced T **cell proliferation** in B10. BR mice (I-Ak, I-Ek) but not in B10.A(4R)(I-Ak,I-E-)mice. These findings indicate that the 46D50V54R and 50V54R generate I-E restricted proliferative responses of T lymphocytes in I-**Eb** /k and I-Ek-carrying mice, resp. Furthermore, it was shown that residue 50 functions as an epitope and residues 46 and 54 as agretopes in the I-E restricted responses. Almost identical results were obtained when I-E restricted responses of T lymphocytes were analyzed in B10.PL(H-2u) and B-10.SM(H-2v)mice. However, since no I-E neg. counterpart strain for these two latter strains is available, complete anal. concerning the epitopic and agretopic functions has not been performed with B10.PL and B10.SM mice. The present findings demonstrated that the functional sites of the p43-58 analogs are preserved in the T cell responses restricted to each I-E haplotype studied. However, when most potent agretopic motif was **detd**. in various mouse strains, the specific amino acid motifs on the agretopic positions were different among various I-E haplotypes. Furthermore, substitution of the epitopic residue showed no influence on the binding affinity between agretopic residues and class II mols. Thus, these epitopes and agretopes appear to function independently. The present findings are essentially consistent with those obtained with I-A restricted T cell responses and may provide basic information for investigating pathogenic **determinant**(s) of the target tissue in **autoimmune diseases** and for designing synthetic vaccines against infectious microorganisms.

L13 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:669015 CAPLUS
DOCUMENT NUMBER: 119:269015
TITLE: A 90 kDa tumor-associated antigen, IR-95, its

purification, and its use in disease treatment and **diagnosis**
INVENTOR(S): Iacobelli, Stefano; Natoli, Clara; Schlessinger, Joseph
PATENT ASSIGNEE(S): New York University, USA; Universita degli Studi "G. D.' Annunzio"-Chieti
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9317119	A2	19930902	WO 1993-EP379	19930216
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9336290	A1	19930913	AU 1993-36290	19930216
CN 1076629	A	19930929	CN 1993-101808	19930217
ZA 9301100	A	19940817	ZA 1993-1100	19930217
PRIORITY APPLN. INFO.:			IT 1992-RM99	19920217
			WO 1993-EP379	19930216

AB The title antigen, which is recognized by monoclonal **antibody** SP-2, is isolated from human breast cancer cell line CG-5, from serum of a breast cancer patient, or from ascites fluid of an ovarian cancer patient. IR-95 is purified by (NH4)2SO4 pptn., size-exclusion chromatog. with Sepharose CL-6B, chromatog. with DEAE-cellulose, and immunoaffinity chromatog. with Sepharose-immobilized monoclonal **antibody** SP-2. The antigen may be used in **diagnosis** or treatment of cancer, viral infection, inflammation, **autoimmune disease**, arthritis, and/or aging (no data). The cDNA for the IR-95 antigen was cloned, sequenced, and expressed in BT-20 breast tumor cells and transiently expressed in 293 cells. Serum IR-95 levels in different pathophysiol. conditions (HIV, hepatitis B, **Epstein-Barr** infection; cancer; **autoimmune disease**; Down syndrome), in pregnancy, aging, and after hemodialysis were **detd**. Levels varied from 1.1 in healthy controls to 1.5-2.7 in various conditions.

L13 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:601321 CAPLUS
DOCUMENT NUMBER: 119:201321
TITLE: Production of anti-endothelial cell **antibodies** by coculture of **EBV**

-infected human B cells with endothelial cells

AUTHOR(S): Delneste, Y.; Lassalle, P.; Jeannin, P.; Mannessier, L.; Dessaint, J. P.; Joseph, M.; Tonnel, A. B.

CORPORATE SOURCE: Contrat Jeune Formation, Inst. Pasteur, Lille, 59019, Fr.

SOURCE: Cell. Immunol. (1993), 150(1), 15-26
CODEN: CLIMB8; ISSN: 0008-8749

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Vascular endothelial cells are suspected of being the target of autoimmune processes seen in many connective tissue diseases and in systemic vasculitis as evidenced by the **detection** of circulating autoantibodies against endothelial cell antigens. To select B cells recognizing endothelial cells antigens, **Epstein-Barr** virus (**EBV**)-infected B cells, obtained from one patient presenting a systemic vasculitis, were cocultured with human endothelial cells concurrently with a human endothelial cell line (EC-pSV1 cells). This coculture consisted of a first step of expansion of B cells specifically selected by adherence onto human umbilical vein endothelial cells (HUVEC). The adherence of selected B cells was specific to endothelial cells because no rosette formation around control cells (HeLa cells or COS cells) was obsd. Adherent B cells were cloned by limiting diln. by coculture onto EC-pSV1 cells and **screened** for anti-HUVEC **antibody** prodn. by endothelial cell ELISA. An increase in anti-HUVEC **antibody** prodn. of IgM isotype was **detected** by endothelial cell ELISA, peaking at day 9 and remaining constantly elevated, relative to B cell expansion. Among 21 B cell lines producing IgM, 6 presented high levels of anti-HUVEC **antibodies**, whereas 1 of 52 B cells cloned without EC-pSV1 cells showed such **antibody** prodn. Anti-HUVEC **antibody** prodn. and B **cell proliferation** were dependent on the presence of endothelial cells. Two of these 6 B cell lines produced **antibodies** directed against an endothelial cell antigen with an apparent mol. wt. of 192 kDa as **detd.** by immunoblotting anal. The authors' results demonstrate that adherence of **EBV**-infected B cells to endothelial cells and further cloning by adherence can efficiently select anti-HUVEC **antibody**-producing human B cells and might help to define antigens potentially involved in **autoimmune diseases**.

L13 ANSWER 25 OF 37 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1993:557810 CAPLUS

DOCUMENT NUMBER: 119:157810

TITLE: Production of anti-endothelial cell **antibodies** by coculture of **EBV**-infected human B cells with endothelial cells

AUTHOR(S): Delneste, Y.; Lassalle, L.; Jeannin, P.; Mannessier, L.; Dessaint, J. P.; Joseph, M.; Tonnel, A. B.
CORPORATE SOURCE: Inst. Pasteur, Lille, 59019, Fr.
SOURCE: Cell. Immunol. (1993), 150(1), 15-26
CODEN: CLIMB8; ISSN: 0008-8749
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Vascular endothelial cells are suspected of being the target of autoimmune processes seen in many connective tissue diseases and in systemic vasculitis as evidenced by the **detection** of circulating autoantibodies against endothelial cell antigens. To select B cells recognizing endothelial cells antigens, **Epstein-Barr** virus (**EBV**)-infected B cells, obtained from one patient presenting a systemic vasculitis, were cocultured with human endothelial cells concurrently with a human endothelial cell line (EC-pSV1 cells). This coculture consisted of a first step of expansion of B cells specifically selected by adherence onto human umbilical vein endothelial cells (HUVEC). The adherence of selected B cells was specific to endothelial cells because no rosette formation around control cells (HeLa cells or COS cells) was obsd. Adherent B cells were cloned by limiting diln. by coculture onto EC-pSV1 cells and **screened** for anti-HUVEC **antibody** prodn. by endothelial cell ELISA. An increase in anti-HUVEC **antibody** prodn. of IgM isotype was **detected** by endothelial cell ELISA, peaking at day 9 and remaining constantly elevated, relative to B cell expansion. Among 21 B cell lines producing IgM, 6 presented high levels of anti-HUVEC **antibodies**, whereas 1 of 52 B cells cloned without EC-pSV1 cells showed such **antibody** prodn. Anti-HUVEC **antibody** prodn. and B **cell proliferation** were dependent on the presence of endothelial cells. Two of these 6 B cell lines produced **antibodies** directed against an endothelial cell antigen with an apparent mol. wt. of 192 kDa as **detd.** by immunoblotting anal. Thus, adherence of **EBV**-infected B cells to endothelial cells and further cloning by adherence can efficiently select anti-HUVEC **antibody**-producing human B cells and might help to define antigens potentially involved in **autoimmune diseases**.

L13 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:189788 CAPLUS
DOCUMENT NUMBER: 118:189788
TITLE: An Fc.gamma.RIII (CD16)-specific autoantibody from a patient with progressive systemic sclerosis
AUTHOR(S): Szegedi, Andrea; Boros, Peter; Chen, Jiayuan; Kaffina, Martin; Bona, Constantin; Unkeless, Jay

C.
CORPORATE SOURCE: Dep. Biochem., Mount Sinai Sch. Med., New York, NY, 10029, USA
SOURCE: Immunol. Lett. (1993), 35(1), 69-76
CODEN: IMLED6; ISSN: 0165-2478
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Polyspecific and organ specific **autoimmune diseases** are often accompanied by prolonged clearance of immune complexes. In mice, impaired macrophage Fc.gamma. receptor function may be assocd. with autoantibody against Fc.gamma. receptors. To extend these observations to **autoimmune** human **disease**, peripheral lymphocytes from a patient with terminal progressive systemic sclerosis were transformed with **EBV** and clones **screened** for secreting anti-Fc.gamma. receptor Ig. A clone, N55, which secretes a high affinity anti-Fc.gamma. receptor IgG2 **antibody** was obtained. The Fab fragment of N55 bound to human neutrophils, NK cells, but not to monocytes, consistent with specificity for Fc.gamma.RIII (CD16). N55 Fab competed weakly for the binding of anti-Fc.gamma.RIII mAb 3G8 to neutrophils but did not have any effect on staining with the anti-Fc.gamma.RII mAb, IV.3. N55 Fab did not bind to peripheral monocytes, but did bind to monocytes incubated with TGF-.beta. (24 h) to induce Fc.gamma.RIII. The specificity of N55 IgG for Fc.gamma.RIII was confirmed by ELISA using secreted recombinant Fc.gamma.RIIA and Fc.gamma.RIIIB protein to coat microtiter wells. N55 IgG triggered the release from neutrophils of .beta.-glucuronidase, aryl-sulfatase, and alk. phosphatase. Such **antibody** may play a pathogenic role in progressive systemic sclerosis.

L13 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1992:126377 CAPLUS
DOCUMENT NUMBER: 116:126377
TITLE: Development and evaluation of a capture ELISA for IgM **antibody** to the human cytomegalovirus major DNA binding protein
AUTHOR(S): Revello, M. Grazia; Percivalle, Elena; Zannino, Marco; Rossi, Valdano; Gerna, Giuseppe
CORPORATE SOURCE: Inst. Infect. Dis., Univ. Pavia, Pavia, 27100, Italy
SOURCE: J. Virol. Methods (1991), 35(3), 315-29
CODEN: JVMEDH; ISSN: 0166-0934
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new capture ELISA (ELAb) for **detn.** of the IgM **antibody** response to the human cytomegalovirus major DNA binding protein (p52) was developed by using a p52-specific monoclonal **antibody**. As a ref. test, a capture ELISA

using in parallel viral- and cell-control labeled antigens (ELA) was employed. General specificity, which was **detd.** on 180 unselected IgM-neg. sera from an adult population was 100%; stringent specificity, which was evaluated on 108 potentially interfering sera from patients with **Epstein-Barr** virus infectious mononucleosis, **autoimmune diseases**, rheumatoid factor or treated with radioimmunotherapy, was 96.3%; finally, clin. specificity, **detd.** on 79 IgM-neg. sera drawn prior to onset of primary HCMV infection, was 100%. Thus, the overall specificity was 98.9% (363/367 IgM neg. tested sera). Sensitivity **assayed** on 277 IgM-pos. sera was 100%. The study of the kinetics of the IgM **antibody** response in sequential blood samples from 9 immunocompetent and 9 heart transplanted patients showed that, while in the immunocompetent p52-specific IgM titer fell sharply 2-3 mo after onset and was virtually undetectable 12 mo after onset, in the immunocompromised the IgM response persisted for longer than a year. Recurrent HCMV infections were assocd. with a high titer IgM response in 6 (30%), and with a low IgM response in another 6 (30%) heart transplanted patients within a group of 20 patients sequentially examd. Finally, IgM **antibodies** were **detected** in all 4 infants with congenital infection and in 5 of 6 infants with neonatal infection. The results show that the HCMV p52-specific IgM **antibody** response parallels that obtained by ELA, thus representing a major component of it. ELAb is highly sensitive, specific and reproducible. It represents a major advance among capture ELISA techniques, allowing **detection** of IgM **antibody** reactive to a specific viral protein.

L13 ANSWER 28 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1992:39673 CAPLUS
DOCUMENT NUMBER: 116:39673
TITLE: Hybrid Fc receptor molecules, their recombinant production, their use, and monoclonal **antibodies** recognizing Fc receptors
INVENTOR(S): Hogarth, Phillip Mark; Hulett, Mark Darren; Ierino, Francesco Libero; McKenzie, Ian Farquhar Campbell; Osman, Narin
PATENT ASSIGNEE(S): University of Melbourne, Australia
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9106570	A1	19910516	WO 1990-AU513	19901025

Searcher : Shears 308-4994

W: AT, AU, BG, BR, CA, CH, DE, DK, ES, FI, GB, GR, HU, JP, LU, NL, NO, RO, SD, SE, SU, US
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG

AU 9066096	A1	19910531	AU 1990-66096	19901025
PRIORITY APPLN. INFO.:			AU 1989-7045	19891025
			WO 1990-AU513	19901025

AB Chimeric Ig-binding mols. derived from Fc receptors (FcR) are provided. The chimeric FcR are derived from bacterial, mammalian, or other origins; they are derived from any 1 of FcR, Fc.gamma.R, Fc.alpha.R, Fc.epsilon.R, Fc.mu.R, or IgE-binding proteins. The chimeric mols. may bind .gtoreq.1 of IgG, IgM, IgA, IgD, or IgE. Sequences of chimeric Fc receptors, and nucleotide sequences encoding them, are included. Thus, chimeric cDNA clones encoding FcR composed of components of different Fc.gamma.R were generated. By connecting D1 and D2 of Fc.gamma.RI to the transmembrane cytoplasmic regions of Fc.gamma.RII, a receptor mol. was produced which had broader specificity than the receptor from which the Ig-binding regions were derived, i.e. Fc.gamma.RI/II contg. D1 and D2 of Fc.gamma.RI binds mouse IgG1, IgG2a, and IgG2b. Prodn. and testing of other chimeric FcR are included, as are prodn. and reactivity of monoclonal **antibodies** (MAbs) to the FcR. Also described is an immunoassay for circulating sol. Fc.gamma.RII in patients with systemic lupus erythematosus, rheumatoid arthritis, and Sjogren syndrome.

L13 ANSWER 29 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1991:556956 CAPLUS
DOCUMENT NUMBER: 115:156956
TITLE: Purification of human membrane cofactor protein (MCP), recombinant production of MCP, and therapeutic and **diagnostic** uses of MCP
INVENTOR(S): Atkinson, John P.
PATENT ASSIGNEE(S): Washington University, USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9102002	A1	19910221	WO 1990-US4107	19900720
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, RO, SD, SE, SU				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CA 2062969	AA	19910122	CA 1990-2062969	19900720

Searcher : Shears 308-4994

AU 9060797	A1	19910311	AU 1990-60797	19900720
AU 651068	B2	19940714		
EP 483247	A1	19920506	EP 1990-911526	19900720
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 05501398	T2	19930318	JP 1990-511085	19900720
JP 2750220	B2	19980513		
US 5514787	A	19960507	US 1992-948350	19920921
US 5552381	A	19960903	US 1994-203867	19940228
AU 9475825	A1	19950427	AU 1994-75825	19941013
AU 679781	B2	19970710		
US 5703046	A	19971230	US 1995-476713	19950607
PRIORITY APPLN. INFO.:			US 1989-384210	19890721
			US 1990-510709	19900419
			WO 1990-US4107	19900720
			US 1992-948350	19920921
			US 1992-984247	19921130

AB Human MCP, a protein involved in regulation of complement activity, has been purified to homogeneity. The cDNAs encoding 6 isoforms of this protein have been retrieved and permit deduction of the complete amino acid sequences and the recombinant prodn. of proteins with this activity. Pharmaceutical compns. in which MCP is the active ingredient for use in treating **autoimmune diseases**, **antibody** prepns. for **diagnosis**, and DNA probes are also disclosed.

L13 ANSWER 30 OF 37 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER:	1991:156804 CAPLUS
DOCUMENT NUMBER:	114:156804
TITLE:	In vitro studies of the effect of MAb NDA 4 linked to toxin on the proliferation of a human **EBV**-transformed lymphoblastoid B cell line and of gibbon MLA-leukemia cell line
AUTHOR(S):	Harris, Paul; Reed, Elaine; King, Donald West; Suciu-Foca, Nicole
CORPORATE SOURCE:	Coll. Physicians Surg., Columbia Univ., New York, NY, 10032, USA
SOURCE:	Cell. Immunol. (1991), 134(1), 85-95 CODEN: CLIMB8; ISSN: 0008-8749
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The rejection of allografts is mediated by cytolytic T cells and **antibody**-secreting B cells. Selective ablation of these activated cells from peripheral blood lymphocytes may offer a method of controlling allograft rejection. An immunotoxin was prepd. from the monoclonal **antibody** (mAb) NDA 4, which recognizes a differentation antigen (NDA 4) common to activated B and T cells. MAb NDA 4 was conjugated to the ribosome-inhibiting protein gelonin via a cleavable disulfide bond provided by a crosslinking reagent. The purified immunotoxin was evaluated for in vitro cytotoxicity on

NDA 4 pos. T and B cell lines. Conjugation of mAb NDA 4 to gelonin increased the in vitro cytotoxicity by a concn. factor of 1000, compared to gelonin alone. The specificity and saturability of mAb NDA 4 binding, as well as the no. of antigenic sites per cell on resting vs. activated T lymphocytes, were also evaluated. Resting T cells expressed 400-800 sites per cell. PHA-activated T cells and the MLA T cell leukemia expressed 10,000 to 80,000 sites per cell. Peripheral blood mononuclear cells obtained from allografted baboons in quiescence or undergoing rejection were compared for NDA 4 expression by flow cytometry. Lymphocytes obtained from baboons rejecting a heart allograft expressed NDA 4, whereas transplant recipients in quiescence showed no **detectable** NDA 4.
These results suggest that mAb NDA 4-derived immunotoxins may be valuable for the selective depletion of activated lymphocytes while sparing the resting population.

L13 ANSWER 31 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1990:476469 CAPLUS
DOCUMENT NUMBER: 113:76469
TITLE: DNA sequences encoding antigenic epitopes of the Ro autoantigen, antigenic peptides, and their use in hybridization **assays** and immunoassays
INVENTOR(S): Sontheimer, Richard D.; Lieu, Tsu San; Capra, J. Donald; McCauliffe, Daniel P.
PATENT ASSIGNEE(S): University of Texas System, USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8909273	A1	19891005	WO 1989-US1213	19890322
W: AT, AU, BB, BG, BR, CH, DE, DK, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, RO, SD, SE, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, FR, GA, GB, IT, LU, ML, MR, NL, SE, SN, TD, TG				
AU 8933405	A1	19891016	AU 1989-33405	19890322
EP 406305	A1	19910109	EP 1989-904325	19890322
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
PRIORITY APPLN. INFO.:			US 1988-171634	19880322
			WO 1989-US1213	19890322

AB DNA sequences encoding .gtoreq.1 antigenic epitope of the Ro 60-kilodalton (kD) autoantigen and antigenic peptides corresponding antigenically to epitopes found on the Ro/SS-A ribonucleoprotein (RNP) particle are disclosed. The peptides may be used in place of

the Ro/SS-A RNP in immunoassays. The DNA sequences may be used to prep. the 60 kD antigen and antigenic peptides or to probe for Ro sequences. A 60-kD protein with Ro antigenic activity was isolated from the **Epstein-Barr** virus-transformed human Wil-2 B-cell line and digested partially with Staphylococcus aureus V8. The amino-terminal ends of 2 fragments were sequenced and the sequence information was used to construct 2 oligonucleotides. A cDNA clone that encoded the protein was then isolated and sequenced. The gene was sequenced and localized to the short arm of chromosome 19. Immobilized peptide ECS-I (Cys-Phe-Lys-Glu-Gln-Phe-Leu-Asp-Gly-Asp-Gly-Trp-Thr-Asp-Arg) reacted with anti-Ro/SS-A antisera but not with autoimmune sera specific for other antigens such as Sm, La/SS-B, and normal human sera.

L13 ANSWER 32 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1990:175253 CAPLUS
DOCUMENT NUMBER: 112:175253
TITLE: Characterization and **detection** of DNA sequences associated with **autoimmune diseases** for **diagnosis** of the same
INVENTOR(S): Erlich, Henry A.; Horn, Glenn T.
PATENT ASSIGNEE(S): Cetus Corp., USA
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 26
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8904875	A2	19890601	WO 1988-US4067	19881114
WO 8904875	A3	19890615		
W: DK, FI, JP, NO				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
JP 03501926	T2	19910509	JP 1989-501309	19881114
EP 439458	A1	19910807	EP 1989-901373	19881114
EP 439458	B1	19940601		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 106454	E	19940615	AT 1989-901373	19881114
JP 2877165	B2	19990331	JP 1988-501309	19881114
CA 1339098	A1	19970729	CA 1988-583260	19881116
US 5665548	A	19970909	US 1995-448021	19950523
PRIORITY APPLN. INFO.:			US 1987-121519	19871117
			US 1986-839331	19860313
			US 1986-899344	19860822
			US 1986-899512	19860822
			EP 1989-901373	19881114

Searcher : Shears 308-4994

WO 1988-US4067 19881114

AB Marker DNA sequences which **detect**, directly or indirectly, the sequence encoding the amino acids assocd. with position 57 of the DQ-.beta.- or DR-.beta.-protein in the HLA class II .beta. region of the human genome are given. The marker DNA sequences are useful as DNA probes or for prepg. **antibodies** to **detect** a person's susceptibility to insulin-dependent diabetes mellitus (IDDM) and pemphigus vulgaris (PV). The resultant **antibodies** can also be used therapeutically or prophylactically. Thus, HLA class II genes were isolated from clin. blood samples of diverse HLA-type IDDM patients by cloning methods and sequenced. The DNA sequences encoding DR-.beta. protein mutants, i.e. alterations of 1-3 amino acid residues in the 2nd exon region, attributed to IDDM were obtained and subjected to amplification to prep. DNA probes. One of the DNA probes (GH78) hybridized to gene samples from PV patients. Homol. of the peptide sequence assocd. with amino acid 57 of the DQ-.beta. allele and **Epstein-Barr** protein was given.

L13 ANSWER 33 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1988:527024 CAPLUS
DOCUMENT NUMBER: 109:127024
TITLE: Comparative biochemical and genetic characterization of clonally related human B-cell lines secreting pathogenic anti-Pr2 cold agglutinins
AUTHOR(S): Silberstein, Leslie E.; Goldman, June; Kant, Jeffrey A.; Spitalnik, Steven L.
CORPORATE SOURCE: Sch. Med., Univ. Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE: Arch. Biochem. Biophys. (1988), 264(1), 244-52
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To study the biol. of cold autoimmune hemolytic anemia, **Epstein-Barr** virus (**EBV**)-transformed B-cell clones were established from a patient with splenic lymphoma assocd. with immune hemolysis due to an anti-Pr2 cold autoantibody. Studies were performed comparing the cold autoantibody present in culture supernatants of these cell lines to the pathogenic cold autoantibodies present in the patient's plasma. Cytogenetic studies of splenic lymphocytes demonstrated an abnormal karyotype (51XX, +3, +9, +12, +13, +18). After **EBV** transformation, eight clones secreting IgM.kappa. anti-Pr were isolated; each clone had the same abnormal karyotype as above. DNA isolated from the clones and spleen was analyzed by Southern blot hybridization with JH, C.mu., and C.kappa. probes; identical gene rearrangements were seen in each case. Anti-Pr **antibodies**, isolated from culture supernatant and serum were compared by isoelec. focusing (IEF) and

demonstrated similar banding patterns. Distinctive banding patterns, however, were obsd. in 2/8 clones, suggesting structural differences. Adsorption studies with red blood cells further showed that the obsd. IEF banding patterns were solely due to anti-Pr cold autoantibody. With a thin-layer chromatog. method, the biochem. **determinants** recognized by the cold autoantibodies were defined as glycolipids contg. Neu Ac.alpha.2-3Gal.beta.1-4Glc sequences. The data demonstrate that the autoantibodies of the **EBV**-transformed B-cell lines were similar to the pathogenic monoclonal serum autoantibody in both structure and specificity. These clonal cell lines may thus serve to further study the biol. of human B-cell lymphomas with defined autoantibody specificity.

L13 ANSWER 34 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1987:634643 CAPLUS
DOCUMENT NUMBER: 107:234643
TITLE: Cell-free T-cell antigen receptor and its **detection** in body fluids by immunoassay for **diagnostic** purposes
INVENTOR(S): Kung, Patrick C.; Ip, Stephen H.; Brown, Michael C.
PATENT ASSIGNEE(S): T Cell Sciences, Inc., USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8703600	A1	19870618	WO 1986-US2591	19861202
W: AU, DK, JP, KR				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4845026	A	19890704	US 1985-804289	19851203
AU 8767725	A1	19870630	AU 1987-67725	19861202
AU 617980	B2	19911212		
EP 248887	A1	19871216	EP 1987-900451	19861202
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 63501721	T2	19880714	JP 1987-500104	19861202
JP 3025271	B2	20000327		
EP 616811	A1	19940928	EP 1994-107605	19861202
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 3025271	B2	20000327	JP 1986-500104	19861202
CA 1304288	A1	19920630	CA 1986-524394	19861203
US 5436319	A	19950725	US 1994-312167	19940926
PRIORITY APPLN. INFO.:			US 1985-804289	19851203
			US 1986-935879	19861201
			EP 1987-900451	19861202

Searcher : Shears 308-4994

WO 1986-US2591 19861202
US 1988-239048 19880830
US 1990-582041 19900912
US 1992-929613 19920813
US 1993-129007 19930929

AB Cell-free T-cell antigen receptors are released from T-cell lines in culture and in individuals with disorders or diseases that involve T-cell responses. These released receptors differ from the cellular membrane-bound receptor and may be used therapeutically or **diagnostically** for certain T-cell malignancies, and other diseases or disorders which elicit or involve T-cell responses, including some infectious **diseases**, cancers, solid tumors, **autoimmune diseases**, allergies, etc. The invention also relates to methods for **detecting** the released T-cell antigen receptor in cell culture supernatants, cell lysates, and human sera. Cell-free T-cell antigen receptor was **detected** in serum of leukemic patients by incubation of the serum in microtiter wells coated with immobilized monoclonal **antibody** to the T3 protein complex of the T-cell membrane. This was followed (washing after each step) by incubation with biotinylated anti-major framework **antibody**, streptavidin-peroxidase conjugate, and chromogen plus H2O2. Serum receptor levels in leukemic patients were .gtoreq.3-fold higher than in normal subjects.

L13 ANSWER 35 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1987:513861 CAPLUS
DOCUMENT NUMBER: 107:113861
TITLE: Synthetic peptide derived from the **Epstein-Barr** virus encoded early diffuse antigen (EA-D) reactive with human **antibodies**
AUTHOR(S): Fox, Robert I.; Scott, Susan; Houghten, Richard; Whalley, Alice; Geltofsky, Jack; Vaughan, John; Smith, Richard
CORPORATE SOURCE: Dep. Bas. Clin. Res., Scripps Clin. and Res. Found., La Jolla, CA, USA
SOURCE: J. Clin. Lab. Anal. (1987), 1(1), 140-5
CODEN: JCANEM; ISSN: 0887-8013
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Primary infection with **Epstein-Barr** virus (**EBV**) and reactivation of latent virus are assocd. with increased **antibody** titers against the diffuse early antigen (EA-D). In order to better define the antigenic epitopes recognized by **antibodies** from patients with infectious mononucleosis (IM) and with other disease states, a series of synthetic peptides were prepd. based on the DNA sequence encoding the EA-D mol. One synthetic peptide (K7b) was reactive with the

majority of sera from patients with acute IM. Anti-K7b activity was most readily **detected** among IgM and IgA **antibodies** and to a lesser extent among IgG **antibodies**. In contrast, significant elevations of anti-K7b activity were obsd. in <5% of healthy adults. Serial anal. of samples from individuals prior to and after exposure to **EBV** demonstrated increased anti-K7b reactivity assocd. with the symptoms of acute IM. Elevated anti-peptide K7b titers also were found in sera of patients with nasopharyngeal carcinoma and with Sjogren's syndrome (an **autoimmune disease** involving the salivary glands). Four different synthetic peptides from other regions of the EA-D mol. were not reactive with **antibodies** from these patients nor from IM patients. Thus, peptide K7b defines an antigenic epitope recognized during primary **EBV** infection and during viral reactivation occurring in patients with **autoimmune** and neoplastic **disease**.

L13 ANSWER 36 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1986:86710 CAPLUS
DOCUMENT NUMBER: 104:86710
TITLE: Molecular analysis of the RNA and protein components recognized by anti-La(SS-B) autoantibodies
AUTHOR(S): McNeilage, L. Jane; Whittingham, Senga; Jack, I.; Mackay, I. R.
CORPORATE SOURCE: Walter Eliza Hall Inst. Med. Res., R. Melbourne Hosp., Melbourne, 3050, Australia
SOURCE: Clin. Exp. Immunol. (1985), 62(3), 685-95
CODEN: CEXIAL; ISSN: 0009-9104
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A study was conducted to **det**. whether sera with autoantibodies to the La(SS-B) nuclear antigen react with the same or different sets of cellular or viral ribonucleoproteins (RNPs) and whether patients with anti-La(SS-B) comprised a homogeneous group with respect to phenotypic and serol. markers. The 34 anti-La(SS-B) sera studied were **detected** in the course of **screening** 2000 sera referred from patients with suspected or defined multisystem **autoimmune disease**. Anal. of the mol. components of the small nuclear (sn) RNPs isolated from immune complexes developed in vitro between the IgG fractions of the anti-La(SS-B) sera and cell lines selected for their content of viral and cellular (non-viral) RNA showed that all 34 anti-La(SS-B) sera reacted with the same group of cellular RNAs and with 2 viral RNAs encoded by **Epstein-Barr** virus. The La(SS-B) RNPs contained 1 major 50,000 dalton antigenic polypeptide that resolved into 5-6 heterogeneously charged isospecies on 2-dimensional immunoblots. In addn. to anti-La(SS-B) reactivity, all 34 sera were shown to contain anti-Ro(SS-A) activity by

counterimmunoelectrophoresis. However, with 3 exceptions, the antigenic Ro(SS-A) polypeptide was not **detectable** by immunoblotting. The homogeneity of this group with anti-La(SS-B) was indicated by the findings that of the 34 cases 31, (88%) had hypergammaglobulinemia, 33 (97%) had rheumatoid factor, and 27 (of 30 tested, 90%) were HLA-B8. Thus, all anti-La(SS-B) sera react with the same set of RNAs assocd. with an antigenic 50,000 dalton nucleoprotein, and the presence of anti-La(SS-B) autoantibodies identified a homogeneous group of patients with the serol. and phenotypic features of primary Sjogren's syndrome.

L13 ANSWER 37 OF 37 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1985:94167 CAPLUS
DOCUMENT NUMBER: 102:94167
TITLE: Human immune responses to synthetic peptides from the **Epstein-Barr** nuclear antigen
AUTHOR(S): Rhodes, Gary; Carson, Dennis A.; Valbracht, Jean; Houghten, Richard; Vaughan, John H.
CORPORATE SOURCE: Dep. Basic Clin. Res., Scripps Clin. Res. Found., La Jolla, CA, 92037, USA
SOURCE: J. Immunol. (1985), 134(1), 211-16
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Humans infected with **Epstein-Barr** virus (**EBV**), the causative agent of infectious mononucleosis, develop **antibodies** against a nuclear antigen (EBNA) that is present in virally transformed B lymphocytes. The EBNA protein contains a unique glycine-alanine repeating sequence. Peptides corresponding to various regions of the EBNA mol. within and near this sequence were synthesized. Rabbit **antibodies** against the peptides within the sequence reacted directly with the EBNA protein, as **detected** by Western blotting. The sera of individuals with **antibodies** against **EBV** contained abundant **antibodies** also reactive with 1 or several of the synthetic peptides within the sequence. Moreover, human **antibodies** against these simple peptides were induced specifically early in the course of infectious mononucleosis. When compared with normal controls, **antibody** levels to the glycine-alanine peptides were significantly higher in patients with rheumatoid arthritis and progressive systemic sclerosis, but not in patients with 2 other **autoimmune diseases**. These results document that i) **antibodies** against the peptides **detect** the EBNA protein, ii) humans infected with **EBV** produce higher titers of **antibodies** reactive with these synthetic antigens, and iii) **antibody** titers against the peptides are abnormally elevated in certain **autoimmune diseases**.

Searcher : Shears 308-4994

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:10:33 ON 06 DEC 2000)

L14 379 S L12

L18 10 S L14 AND REAGENT
L19 10 DUP REM L18 (0 DUPLICATES REMOVED)

L19 ANSWER 1 OF 10 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000-611626 [58] WPIDS
CROSS REFERENCE: 2000-422855 [36]; 2000-422864 [36]; 2000-490499 [35]
DOC. NO. CPI: C2000-183059
TITLE: Use of new and known androstan-17-one derivatives as immunomodulators to treat, prevent and delay e.g. viral, bacterial, fungal and protozoal infections, cancers, wounds, burns, Crohn's **disease**, diabetes and **autoimmune diseases**.
DERWENT CLASS: B01 C03
INVENTOR(S): AHLEM, C N; DE CARVALHO, L D D A; FRINCKE, J M; HEGGIE, W; PRENDERGAST, P T; READING, C L; THADIKONDA, K P; VERNON, R N
PATENT ASSIGNEE(S): (HOLL-N) HOLLIS-EDEN PHARM INC
COUNTRY COUNT: 91
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000056757	A1	20000928	(200058)*	EN	244

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000056757	A1	WO 2000-US7883	20000323

PRIORITY APPLN. INFO: US 1999-164048 19991108; US 1999-126056 19990323; US 1999-140028 19990616; US 1999-414905 19991008
AN 2000-611626 [58] WPIDS
CR 2000-422855 [36]; 2000-422864 [36]; 2000-490499 [35]

Searcher : Shears 308-4994

AB WO 200056757 A UPAB: 20001114
NOVELTY - Compositions contain new and known androstan-17-one derivatives

DETAILED DESCRIPTION - Compositions contain androstane derivatives of formula (I), one or more nonaqueous liquid excipients and less than 3 % v/v water.

R1-R6, R10 = H, ORPR, SRPR, N(RPR)2, OSi(R13)3, CN, NO2, ester, thioester, phosphoester, phosphothioester, phosphonoester, phosphiniester, sulfite ester, sulfate ester, amide, amino acid, peptide, ether, thioether, acyl, thioacyl, carbonate, carbamate, thioacetal, halo or alkyl, alkenyl, alkynyl, aryl, heteroaryl or mono- or disaccharide (all optionally substituted) or nucleoside, nucleotide, oligonucleotide or polymer or oxo or thioxo (in both cases with the other H atom missing); or

R3+R4+R4 = residue of ring D' which is a heterocycle (i) or a 4-7-membered ring (ii) comprising saturated C atoms, where 1-3 ring C atoms in (ii) are optionally substituted by O, S or NRPR, and where 1-3 H atoms in (i) or 1-2 H atoms in (ii) are substituted by R1, or D' is two 5-6-membered rings which are fused or linked by 1 or 2 bonds;

R7 = CHR10, (CHR10)2, (CHR10)3, CHR10OCHR10, CHR10SCHR10, CHR10N(RPR)CHR10, O, OCHR10, S, SCHR10, N(RPR) or N(RPR)CHR10;

R8, R9 = CHR10, (CHR10)2, O, OCHR10, S, SCHR10, N(RPR), N(RPR)CHR10 or bond;

R13 = 1-6C alkyl; and

a, b, c = single or double bonds.

RPR, R10 are not defined.

INDEPENDENT CLAIMS are included for:

(1) 16 alpha -bromo-3 beta -hydroxy-5 alpha -androstan-17-one hemihydrate (I'') substantially free of other forms of 16 alpha -bromo-3 beta -hydroxy-5 alpha -androstan-17-one; and

(2) compounds of formula (I')

R3, R4 = as in (I); or

R3+R4 = residue of D'.

ACTIVITY - Immunostimulant; immunosuppressive; immunomodulator; virucide; antibacterial; protozoacide; fungicide; cytostatic; vulnerary; antiinflammatory; antidiarrheic; antiarthritic; antidiabetic; anti-HIV. When **assayed** for in vitro inhibition of Plasmodium falciparum, (I'') showed 98 % inhibition compared to 60 % for etienic acid methyl ester.

MECHANISM OF ACTION - None given.

USE - The compounds are used to enhance a Th1 immune response or reduce a Th2 response, both associated with viral infections, intracellular and extracellular bacterial and parasitic infections, fungal and yeast infections, protozoal and multicellular parasite infections, **autoimmune diseases**, malignancy or precancer, chemotherapy, immunosuppressive therapy, anti-infective agent therapy, wounds, burns, the presence of an immunosuppressive molecule and/or gastrointestinal irritation or inflammation. They

are used to treat, prevent or delay DNA and RNA virus infections (selected from HSV, CMV, HBV, HCV, HIV, SIV, SHIV, FIV, **EBV**, HSV-1, -2 and -6, HHV-6 and -8, adeno-associated virus, measles virus, poxvirus, Poliovirus, human rhinovirus, and human and animal papilloma virus), mycoplasma, Listeria, Mycobacterium, Streptococcus, Staphylococcus, Vibrio, Salmonella, Shigella, enterotoxigenic, enteropathogenic, enteroinvasive or enterohemorrhagic E. coli, Yersinia, Campylobacter, Pseudomonas, Borrelia, Legionella and Haemophilus infections, pulmonary Aspergillosis infections, mucosal or oropharyngealcandidiasis and juvenile paracoccidiomycosis, Candida and Cryptococcus infections, systemic lupus erythematosis, arthritis, diabetes, solid or disseminated cancers (selected from ovarian, cervical, breast and prostate cancer, liver cancer or carcinoma, glioma, lymphoma, leukemia and colon cancer), benign prostatic hyperplasia, recurrent condylomata acuminata, surgical and accidental wounds, irritable bowel disease, Crohn's disease, chronic diarrhea and/or side effects associated with treatment with adriamycin, cisplatin, mitomycin C, amphotericin B, gamma -radiation, nucleoside analogs, cyclosporin and corticosteroids. They are also used to treat one or more complications or co-infections associated with AIDS, and to treat a pathogen infection or malignancy where at least 30 % of patients do not develop resistance over the time in which resistance develops for prior art treatments. (I) are used to enhance the expression of **cytokines** or interleukins (selected from IL-2, IL-12 or gamma -IFN) that facilitate Th1 responses and to reduce the expression of **cytokines** (selected from IL-4 or IL-10) that reduce Th2 responses (all claimed).

ADVANTAGE - Patients develop resistance to (I) and (I') over a longer period than to prior art drugs.

Dwg.0/0

L19 ANSWER 2 OF 10 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1998-399062 [34] WPIDS
DOC. NO. NON-CPI: N1998-310434
DOC. NO. CPI: C1998-120903
TITLE: Use of **Epstein-Barr** virus or component(s) - for developing product(s) which can be used for preventing, **diagnosing**, treating or **determining** risk of developing **autoimmune disease**.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): HARLEY, J B; JAMES, J A
PATENT ASSIGNEE(S): (OKLA-N) OKLAHOMA MEDICAL RES FOUND
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 9830586 A2 19980716 (199834)* EN 80
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9860185 A 19980803 (199850)
EP 1007552 A2 20000614 (200033) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9830586	A2	WO 1998-US342	19980113
AU 9860185	A	AU 1998-60185	19980113
EP 1007552	A2	EP 1998-903405	19980113
		WO 1998-US342	19980113

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9860185	A	Based on	WO 9830586
EP 1007552	A2	Based on	WO 9830586

PRIORITY APPLN. INFO: US 1997-781296 19970113
AN 1998-399062 [34] WPIDS
AB WO 9830586 A UPAB: 19980826
A vaccine for alleviating or preventing **autoimmune disorders** induced by infection with **Epstein-Barr** virus (**EBV**), comprises **EBV** or a component in a carrier for administration of the virus or viral component to alleviate or prevent the **autoimmune disorder**.

Also claimed are: (1) a **diagnostic** test kit comprising: (a) **reagents** which can be used to **detect** levels of **antibodies** to **EBV**, indicators of **EBV** infection of cells, or levels of **EBV** DNA or protein in a patient; (b) control samples from individuals not at risk of developing an **autoimmune disease**; and (c) a device for **determining** the differences in levels of a patient and control samples to distinguish individuals at higher risk of developing an **autoimmune disease** from those at lower risk of developing an **autoimmune disease**; and (2) a method for **screening** for genetic markers or risk factors for development of **autoimmune disorders** induced by infection with **EBV** comprising comparing the responses of different strains of the same species of an animal vaccinated with **EBV** or a component to induce an autoimmune response in at least one of the strains and comparing the differences in the

genetics of the different strains to identify potential genetic markers or risk factors.

USE - The methods can be used for the prevention, **diagnosis**, and treatment of **autoimmune diseases** having **EBV** as an etiological agent. The **autoimmune diseases** may be e.g. systemic lupus erythematosus, Sjogren's syndrome, rheumatoid arthritis, juvenile onset diabetes mellitus, Wegener's granulomatosis, inflammatory bowel disease, polymyositis, dermatomyositis, multiple endocrine failure, Schmidt's syndrome, **autoimmune** uveitis, Addison's **disease**, adrenalitis, primary biliary cirrhosis, Graves' disease, thyroiditis, Hashimoto's thyroiditis, **autoimmune** thyroid **disease**, pernicious anaemia, lupoid hepatitis demyelating diseases, multiple sclerosis, subacute cutaneous lupus erythematosus, hypoparathyroidism, Dressler's syndrome, myasthenia gravis, autoimmune thrombocytopenia, idiopathic thrombocytopenic purpura, haemolytic anaemia, autoimmune haemolytic anaemia, pemphigus vulgaris, pemphigus, bullous pemphigoid, dermatitis herpetiformis, alopecia areata, autoimmune cystitis, pemphigoid scleroderma, progressive systemic sclerosis, CRST syndrome (a subset of progressive system sclerosis consisting of calcinosis, Raynaud's phenomenon, esophageal dysmotility sclerodactyly and telangiectasia), adult onset diabetes mellitus (Type II diabetes), male or female autoimmune infertility, ankylosing spondylitis, ulcerative colitis, Crohn's disease, mixed connective tissue disease, polyarteritis nodosa, systemic necrotising vasculitis, juvenile onset rheumatoid arthritis, glomerulonephritis, atopic dermatitis, atopic rhinitis, Goodpasture's syndrome, Chagas disease, sarcoidosis, rheumatic fever, asthma, recurrent abortion, anti-phospholipid syndrome, farmer's lung, erythema multiforme, postcardotomy syndrome, Cushing's syndrome, autoimmune chronic active hepatitis, bird-fancier's lung, allergic encephalomyelitis, toxic necrodermal lysis, alopecia, Alport's syndrome, alveolitis, allergic alveolitis, fibrosing alveolitis, interstitial lung disease, erythema nodosum, pyoderma gangrenosum, transfusion reaction, chronic fatigue syndrome, fibromyalgia, Takayasu's arteritis, Kawasaki's disease, polymyalgia rheumatica, temporal arteritis, giant cell arteritis, Sampter's syndrome (triaditis also called, nasal polyps, eosinophilia and asthma), Behcet's disease, Captan's syndrome, dengue, encephalomyositis, endocarditis, myocarditis- endomyocardial fibrosis, endophthalmitis, erythema elevatum et diutinum, psoriasis, erythroblastosis fetalis, fascitis with eosinophilia, Shulman's syndrome, Felty's syndrome, filariasis, cyclitis, chronic cyclitis,chronic cyclitis, heterochromic cyclitis, Fuch's syslitis, IgA nephropathy, Henoch-Schonlein purpura, glomerulonephritis, cardiomyopathy, post vaccination syndromes, Hodgkin's and non-Hodgkin's lymphoma, renal cell carcinoma, Eaton-Lambert syndrome, or relapsing polychondritis.

Dwg.0/8

L19 ANSWER 3 OF 10 JICST-EPlus COPYRIGHT 2000 JST
ACCESSION NUMBER: 990186305 JICST-EPlus
TITLE: Development of evaluation technology of biotechnology applied extracorporeal **diagnostic reagent** for the **diagnosis** of herpes virus infection. (Human science promotion foundation S).
AUTHOR: YANAGI ICHIO
CORPORATE SOURCE: Kansenshoken
SOURCE: Kanmin Kyodo Purojekuto Kenkyu Hokoku. Heisei 9 Nendo. Dai1 Bun'ya. Raifusaiensu no Kiso to shiteno Baiotekunoroji no Oyo to Hyoka Gijutsu no Kaihatsu, (1998) pp. 94-100. Journal Code: N19990012 (Fig. 2)
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New

L19 ANSWER 4 OF 10 JICST-EPlus COPYRIGHT 2000 JST
ACCESSION NUMBER: 970741948 JICST-EPlus
TITLE: Development of evaluation technology for extracorporeal **diagnostic reagents** applied with biotechnology for **diagnosis** of herpes virus infection. (Human Sience Promotion Foundation S).
AUTHOR: YANAGI ICHIO
ISHIMATSU YOSHIAKI
CORPORATE SOURCE: Kansenshoken
Denka Seiken Co., Ltd.
SOURCE: Kanmin Kyodo Purojekuto Kenkyu Hokoku. Heisei 8 Nendo. Dai1 Bun'ya. Raifu Saiensu no Kiso to shiteno Baiotekunoroji no Oyo to Hyoka Gijutsu no Kaihatsu, (1997) pp. 100-106. Journal Code: N19972025 (Fig. 3, Tbl. 1)
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New

L19 ANSWER 5 OF 10 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 96:357974 SCISEARCH
THE GENUINE ARTICLE: UH854
TITLE: SELECTION OF LIGANDS FOR POLYCLONAL **ANTIBODIES** FROM RANDOM PEPTIDE LIBRARIES - POTENTIAL IDENTIFICATION OF (AUTO)ANTIGENS THAT MAY TRIGGER B-CELL AND T-CELL RESPONSES IN **AUTOIMMUNE-DISEASES**
AUTHOR: SIOUD M (Reprint); FORRE O; DYBWAD A

CORPORATE SOURCE: UNIV OSLO, INST IMMUNOL & RHEUMATOL, FR QUAMSGT 1, N-0172 OSLO, NORWAY (Reprint)
COUNTRY OF AUTHOR: NORWAY
SOURCE: CLINICAL IMMUNOLOGY AND IMMUNOPATHOLOGY, (MAY 1996) Vol. 79, No. 2, pp. 105-114.
ISSN: 0090-1229.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 65

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The development of random peptide libraries has increased our possibility for analyzing the structural features involved in binding events. Recently, reports have appeared in which these libraries have been successfully used to investigate binding properties of homogeneous proteins such as monoclonal **antibodies**. However, a more general application of peptide libraries would be the use of polyclonal sera or fluids from patients with **autoimmune diseases** in biopanning experiments. This would subsequently allow the identification of (auto)antigen leads responsible for the initiation and/or perpetuation of the immune response in these patients. Moreover, the strategy allows the structural characterization of autoantibody specificities in body fluids that have been produced in vivo without the introduction of bias due to preferential B cell growth under in vitro conditions. The application of this novel strategy for selection of **antibody** ligands for polyclonal sera as well as to study the nature of immune responses to defined proteins will be discussed with emphasis on the development of peptide **reagents** for **diagnostic** and vaccine use. (C) 1996 Academic Press, Inc.

L19 ANSWER 6 OF 10 JICST-EPlus COPYRIGHT 2000 JST
ACCESSION NUMBER: 961013478 JICST-EPlus
TITLE: Development of evaluation technology of biotechnology application drugs. Development of evaluation technology of biotechnology application extracorporeal **diagnostic reagent** for **diagnosing** herpes virus infection . (Human Science Promotion Foundation S)
AUTHOR: YANAGI KAZUO
CORPORATE SOURCE: National Inst. of Health
SOURCE: Kanmin Kyodo Purojekuto Kenkyu Hokoku. Heisei 7 Nendo. Dai1 Bun'ya. Raifu Saiensu no Kiso to shiteno Baiotekunoroji no Oyo to Hyoka Gijutsu no Kaihatsu, (1996) pp. 93-96. Journal Code: N19962646 (Fig. 2)
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese

STATUS: New

L19 ANSWER 7 OF 10 MEDLINE
ACCESSION NUMBER: 89008795 MEDLINE
DOCUMENT NUMBER: 89008795
TITLE: Performance and reliability of five commercial enzyme-linked immunosorbent **assay** kits in **screening** for anti-human immunodeficiency virus **antibody** in high-risk subjects.
AUTHOR: Ozanne G; Fauvel M
CORPORATE SOURCE: Laboratoire de sante publique du Quebec, Canada..
SOURCE: JOURNAL OF CLINICAL MICROBIOLOGY, (1988 Aug) 26 (8) 1496-500.
Journal code: HSH. ISSN: 0095-1137.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198901
AB Anti-human immunodeficiency virus enzyme-linked immunosorbent **assay** kits marketed by Electro-Nucleonics Inc. (ENI), Genetic Systems Corp. (GSC), Organon Teknika Inc. (OTI), Ortho **Diagnostic** Systems Inc. (ODSI), and Wellcome **Diagnostics** (WD) were evaluated by using 289 randomly selected serum samples from a high-risk population and 53 serum samples likely to produce false-positive results. The radioimmunoprecipitation **assay** was used as the reference test. Sensitivities ranged from 96.51% (ODSI, WD) to 97.67% (ENI, GSC, OTI). Sera showing **antibodies** to viral glycoproteins only produced the false-negative results. Specificities ranged from 99.6% (ENI, GSC, ODSI, OTI) to 100% (WD). False-positive results were obtained with sera from patients with **autoimmune disease** or **Epstein-Barr** virus infection.
Only results from GSC and OTI kits were distributed in two compact clusters well segregated on either side of the cutoff point. ODSI and GSC kits had the best intralot reproducibility. The GSC kit had the best interlot reproducibility. Cutoff values for ODSI and GSC kits were the least variable. Intraplate repeatability was good for all kits. Sample localization was not an important source of variability. Our results do not point out one outstanding kit among the five evaluated. However, the GSC kit showed the best overall results.

L19 ANSWER 8 OF 10 JICST-EPlus COPYRIGHT 2000 JST
ACCESSION NUMBER: 880589194 JICST-EPlus
TITLE: Measurement of **EBV antibodies**. Comparison between immunoperoxidase **assay** and immunofluorescence **assay**.
AUTHOR: TAJIMA MASAKO; TAKEDA FUMIKO; YASUDA KAZUTO

OKINAGA KIMIE
CORPORATE SOURCE: Teikyo Univ., School of Medicine
Okinagakurinikku
SOURCE: Kansenshogaku Zasshi (Journal of the Japanese Association for Infectious Diseases), (1988) vol. 62, no. 9, pp. 798-804. Journal Code: Z0760A (Fig. 6, Tbl. 1, Ref. 10)
ISSN: 0387-5911
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New

AB It is well established that the **Epstein-Barr** virus(**EBV**) is a causative agent for infectious mononucleosis and that the **EBV** is strongly associated with Burkitt lymphoma and nasopharyngeal carcinoma. For the serological **detection** and titration of specific **EBV**/VCA **antibody** in human serum. Immunofluorescence **Assay** has been most commonly used to **detect** the **antibodies** against **EBV** and its related **antibodies**. The following results were obtained by comparison of indirect immunoperoxidase **assay**(IPA) using the IPAzyme kit and indirect immunofluorescense **assay**(IFA) for the sensitive and specific **determination** of **EBV** and its related **antibodies**. 1) In the **detection** of anti-VCA IgG **antibodies**, the correlation coefficient between IFA and IPA was 0.51. When it is assumed that the error range is plus or minus 1 dilution is the serial dilutions, 41% sera did not show the same **antibody** titer in both IFA and IPA. In IPA, 26.3% sera (7 patients with IM, 2 patients with enlarged liver and spleen, one patient with chronic **EBV** infection) showed a higher **antibody** titer than in IFA by more than 2 dilutions. In IFA, 14.3% sera (2 patients with leukemia, one patient with hepatitis) showed a higher **antibody** titer than in IPA by more than 2 dilutions. 2) In the **detection** of IgM **antibodies**, 42.7% sera did not show the same **antibody** titer between IFA and IPA. However, in the case of patients with **autoimmune disease**, most sera were positive for IgM **antibodies** in IFA whereas they were negative in IPA. Thus, a great difference was observed, which was due to the non-specific reaction commonly seen in the patients with autoimmune deseases.(abridged author abst.)

L19 ANSWER 9 OF 10 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 88212979 EMBASE
DOCUMENT NUMBER: 1988212979
TITLE: B cell clones in rheumatoid arthritis.
AUTHOR: Steinitz M.

CORPORATE SOURCE: Department of Pathology, The Hebrew University, Hadassah Medical School, Jerusalem, Israel
SOURCE: Springer Seminars in Immunopathology, (1988) 10/2-3 (181-188).
ISSN: 0344-4325 CODEN: SSIMDV
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Monoclonal **antibodies** generated by in vitro growing cell lines which are derived from rheumatoid arthritis patients are important tools in helping to understand **autoimmune diseases**. The fact that only very few such B cell lines were established is due to technical problems. **EBV** was successfully applied to immortalize rheumatoid factor-producing lymphocytes giving rise to stable IgM autoimmune **antibody** -producing lymphoblastoid cell line. It is evident that rheumatoid factor-committed lymphocytes reside in various cell populations and that their engendered autoimmune **antibodies** differ. There is a need to establish more B cell lines from rheumatoid arthritis to cover a wider repertoire of autoimmune **antibodies**. These in vitro-produced monoclonal rheumatoid factors would in turn be excellent material for amino acid sequence study and for the preparation of antiidiotypes. The latter **reagents** can clarify the degree of similarity and conserved **determinants** in the combining site of poly- and monoclonal rheumatoid factors derived from patients and also from healthy subjects. Elucidation of these questions might help clarify the normal physiological role which these autoimmune **antibodies** play in the immune response. Moreover, the possible conserved **determinant**(s) of the various rheumatoid factors might give the clue to the initial immunogen, which leads in vivo to hyperproduction of rheumatoid factors.

L19 ANSWER 10 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1982:38312 BIOSIS
DOCUMENT NUMBER: BR22:38312
TITLE: MONO CLONAL RHEUMATOID FACTOR PRODUCED IN-VITRO BY **EPSTEIN BARR** VIRUS CELL LINE A **REAGENT** TO **DETECT** TUMOR ANTIGENS AND SPECIFIC **ANTIBODIES**.
AUTHOR(S): STEINITZ M; TAMIR S
CORPORATE SOURCE: DEP. HEMATOL., HADASSAH UNIV. HOSP., JERUSALEM 91120, ISR.
SOURCE: 10TH ANNUAL MEETING OF THE INTERNATIONAL SOCIETY FOR EXPERIMENTAL HEMATOLOGY, MUNICH, WEST GERMANY, AUG. 23-27, 1981. EXP HEMATOL (LAWRENCE), (1981) 9 (SUPPL

9), 48.
CODEN: EXHMA6. ISSN: 0301-472X.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

Claim 10

FILE 'CAPLUS' ENTERED AT 15:24:10 ON 06 DEC 2000
L20 67 SEA ABB=ON PLU=ON (EBV OR EB OR EPSTEIN BARR) AND (SLE OR SYSTEM? LUPUS)
L21 30 SEA ABB=ON PLU=ON L20 AND (DIAGNOS? OR DETERM? OR DETECT? OR DET## OR SCREEN? OR ASSAY?)
L22 22 SEA ABB=ON PLU=ON L21 NOT (L3 OR L13)

L22 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:390986 CAPLUS
TITLE: Specificity of anti-phospholipid antibodies in infectious mononucleosis: a role for anti-cofactor protein antibodies
AUTHOR(S): Sorice, M.; Pittoni, V.; Griggi, T.; Losardo, A.; Leri, O.; Magno, M. S.; Misasi, R.; Valesini, G.
CORPORATE SOURCE: Dipartimento di Medicina Sperimentale e Patologia, Universita "La Sapienza", Rome, 00161, Italy
SOURCE: Clin. Exp. Immunol. (2000), 120(2), 301-306
CODEN: CEXIAL; ISSN: 0009-9104
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antigen specificity of anti-phospholipid antibodies in infectious mononucleosis (IM) was studied using ELISA for the **detection** of anti-.beta.2-glycoprotein I (.beta.2-GPI), anti-annexin V, anti-protein S and anti-prothrombin antibodies and TLC immunostaining for the **detection** of anti-phospholipid antibodies. This technique enabled us to look at antibodies reacting to "pure" phospholipid antigens in the absence of protein contamination. Sera from 46 patients with IM, 18 with **systemic lupus** erythematosus (**SLE**), 21 with primary anti-phospholipid antibody syndrome (PAPS), 50 with Helicobacter pylori infection and 30 healthy blood donors were tested. This study highlights anti-phospholipid antibodies in patients with IM as specific "pure" anti-cardiolipin antibodies, while in PAPS and **SLE** patients anti-phosphatidylserine and anti-phosphatidylethanolamine antibodies were also found. This investigation also shows that the anti-cardiolipin antibodies found in IM can be present with anti-cofactor protein antibodies. The higher prevalence of anti-cofactor antibodies found in IM sera than in Helicobacter pylori sera may be due to the immunostimulatory

effect and/or the polyclonal activation often obsd. in course of **Epstein-Barr** virus infection. However, anti-.beta.2-GPI and, to a lesser extent, anti-prothrombin antibodies occur with a significantly lower prevalence in IM than in PAPS patients. This finding suggests that these antibodies should be regarded as the expression of the broad autoimmune syndrome involving the phospholipid-binding plasma proteins.

REFERENCE COUNT: 44
REFERENCE(S):
(1) Abuaf, N; Thromb Haemost 1997, V77, P856 CAPLUS
(2) Arvieux, J; Thromb Haemost 1995, V74, P1120 CAPLUS
(3) Celli, C; Biochim Biophys Acta 1999, V1416, P225 CAPLUS
(5) Forastiero, R; Thromb Haemost 1996, V75, P717 CAPLUS
(6) Guermazi, S; Thromb Res 1997, V86, P197 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:246501 CAPLUS
DOCUMENT NUMBER: 131:43356
TITLE: Antibodies against **Epstein Barr** virus in sera of patients with rheumatoid arthritis
AUTHOR(S): Zhang, Xingmin; Li, Baomin; Liu, Yongjie; Jiang, Ming
CORPORATE SOURCE: Department of Rheumatology, PUMC Hospital, CAMS and PUMC, Beijing, 100730, Peop. Rep. China
SOURCE: Zhongguo Yixue Kexueyuan Xuebao (1999), 21(1), 8-12
CODEN: CIHPDR; ISSN: 1000-503X
PUBLISHER: Zhongguo Yixue Kexueyuan
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The relationship between the infection of **Epstein-Barr** virus (**EBV**) and the pathogenesis of rheumatoid arthritis (RA) was studied. The IgA and IgG antibodies against **EBV** capsid antigen (IgA/VCA and IgG/VCA resp.), and anti-Z protein IgG antibodies (IgG/Z) in the sera from the patients with RA, **systemic lupus** erythematosus (**SLE**), and normal controls were **detd**. by indirect immunofluoresence and immunobloting techniques. The pos. rate of IgA/VCA antibody in the serum of RA patients was higher than those in **SLE** patients and normal subjects. The anti-IgG/Z antibodies were only found in RA patients with IgA/VCA antibody. Thus, activated **EB** virus may play a role in the pathogenesis of RA. And it is a useful method for the clin.

diagnosis of RA.

L22 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:471019 CAPLUS
DOCUMENT NUMBER: 129:243959
TITLE: Peripheral blood T cells and monocytes and B cell lines derived from patients with lupus express estrogen receptor transcripts similar to those of normal cells
AUTHOR(S): Suenaga, Ronsuke; Evans, Marilyn J.; Mitamura, Ko; Rider, Virginia; Abdou, Nabih I.
CORPORATE SOURCE: Immunology Research Laboratory, St. Luke's Hospital, University of Missouri, Kansas, MO, 64111, USA
SOURCE: J. Rheumatol. (1998), 25(7), 1305-1312
CODEN: JRHUA9; ISSN: 0315-162X
PUBLISHER: Journal of Rheumatology Publishing Co. Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this report, the authors identified and characterized estrogen receptor (ER) transcripts expressed in immune cells of patients with **systemic lupus** erythematosus (**SLE**) and healthy donors. Peripheral blood monocytes and T cells were prepd. from patients with **SLE** and healthy donors. T cells were sepd. into CD4 and CD8. Some monocytes and T cells were stimulated with estradiol, PMA, and ionomycin. **Epstein-Barr** virus-transformed B cell lines and B cell hybridomas established from patients with **SLE** and a healthy individual were used as a B cell source. These cells were examd. for ER mRNA by reverse transcription nested polymerase chain reaction. Amplified cDNA were sequenced by std. methods. In all cells tested, ER mRNA was expressed without prior in vitro stimulation. Partial sequences from exons 1-8 were nearly identical to the published sequence of the human ER mRNA. There were no notable differences in the ER transcripts between patients and healthy controls. Variant receptor transcripts lacking exon 5 or exon 7, which encodes the hormone binding domain, were identified in the majority of the cells. Precise deletion of the exons suggests that they are alternatively spliced transcripts. Whether the **detected** transcripts are translated into functional receptor proteins remains to be **detd.** In vitro stimulation did not affect ER mRNA expression. The presence of variants did not correlate with disease activity or medication. Thus, monocytes, T cells, and B cells in patients express transcripts of the normal wild type ER and the hormone binding domain variants in vivo.

L22 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:808801 CAPLUS
TITLE: An increased prevalence of **Epstein-**

Barr virus infection in young patients suggests a possible etiology for **systemic lupus** erythematosus

AUTHOR(S): James, Judith A.; Kaufman, Kenneth M.; Farris, A. Darise; Taylor-Albert, Elizabeth; Lehman, Thomas J. A.; Harley, John B.

CORPORATE SOURCE: Department of Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 73104, USA

SOURCE: J. Clin. Invest. (1997), 100(12), 3019-3026
CODEN: JCINAO; ISSN: 0021-9738

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An unknown environmental agent has been suspected to induce **systemic lupus** erythematosus (lupus) in man. Prompted by our recent immunochem. findings, we sought evidence for an assocn. between **Epstein-Barr** virus infection and lupus. Because the vast majority of adults have been infected with **Epstein-Barr** virus, we chose to study children and young adults. Virtually all (116 of 117, or 99%) of these young patients had seroconverted against **Epstein-Barr** virus, as compared with only 70% (107 of 153) of their controls (odds ratio 49.9, 95% confidence interval 9.3-1025, P < 0.00000000001). The difference in the rate of **Epstein-Barr** virus seroconversion could not be explained by serum IgG level or by cross-reacting anti-Sm/nRNP autoantibodies. No similar difference was found in the seroconversion rates against four other herpes viruses. An **assay** for **Epstein-Barr** viral DNA in peripheral blood lymphocytes established **Epstein-Barr** virus infection in the peripheral blood of all 32 of the lupus patients tested, while only 23 of the 32 matched controls were infected (odds ratio > 10, 95% confidence interval 2.53-.infin., P < 0.002). When considered with other evidence supporting a relationship between **Epstein-Barr** virus and lupus, these data are consistent with, but do not in themselves establish, **Epstein-Barr** virus infection as an etiol. factor in lupus.

L22 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1997:84461 CAPLUS

DOCUMENT NUMBER: 126:156232

TITLE: Cross-reactivity of human IgG anti-F(ab')2 antibody with DNA and other nuclear antigens

AUTHOR(S): Williams, Ralph C.; Malone, Christine C.; Cimbalnik, Kelly; Presley, Matthew A.; Roux, Kenneth H.; Strelets, Lioudmila; Silvestris, Franco

CORPORATE SOURCE: University of Florida School of Medicine,

Gainesville, FL, USA
SOURCE: Arthritis Rheum. (1997), 40(1), 109-123
CODEN: ARHEAW; ISSN: 0004-3591
PUBLISHER: Lippincott-Raven
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors characterized the immunol. specificity and possible antiidiotype activity of IgG anti-F(ab')2 in normal subjects as well as in patients with active and inactive **systemic lupus** erythematosus (**SLE**). IgG anti-F(ab')2 and anti-double-stranded DNA (anti-dsDNA) were affinity isolated from immunoadsorption columns of F(ab')2 and dsDNA linked to Sepharose 4B. Affinity-purified IgG anti-F(ab')2 (APAF) and affinity-isolated IgG anti-dsDNA (APAD) were tested by ELISA for other cross-reacting specificities including anti-Sm, anti-Sm/RNP, and anti- Crithidia binding. Anti-DNA specificity of APAF and APAD was **assayed** by S1 nuclease treatment of heat-denatured DNA. Rabbit antiidiotypic antisera were prepd. by immunization with APAF and APAD from normal subjects and **SLE** patients and absorption with insolubilized human Cohn fraction II (FrII). VL and VH regions of 5 monoclonal IgM antibodies with anti-F(ab')2/anti-DNA specificity generated by **Epstein-Barr** virus B cell stimulation were sequenced by polymerase chain reaction and characterized for VH and VL subgroup. APAF and APAD were also examd. by high-resoln. electron microscopy for possible ring forms indicative of antiidiotypic V-region interactions. APAF from normal subjects, representing 0.08-0.18% of serum IgG, showed striking relative concns. of both anti-F(ab')2 and anti-DNA, as well as anti-Sm and anti-Sm/RNP ELISA reactivity. Both APAF and APAD reacting with F(ab')2 or dsDNA on the ELISA plate could be cross-inhibited by F(ab')2 or DNA in soln. Anti-DNA reactivity in normal APAF and APAD was much more sensitive to S1 nuclease treatment than similar fractions from **SLE** patients. Neither APAF nor APAD from controls produced pos. antinuclear immunofluorescence or pos. Crithidia staining, whereas these were strongly pos. using **SLE** APAF and APAD. Absorbed rabbit antisera against normal or **SLE** APAF and APAD showed strong ELISA reactivity against both APAF and APAD, but no residual reactivity with normal FrII. VL and VH sequencing of monoclonal human IgM antibodies showing both anti-F(ab')2 and anti-DNA reactivity showed relative VH3, Vk1 or VH1, Vk3 restriction. No evidence of ring forms or V-region "kissing" dimers was obtained when normal or **SLE** APAD or APAF was examd. by high-resoln. electron microscopy.

L22 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:538155 CAPLUS
DOCUMENT NUMBER: 125:245420
TITLE: An **Epstein Barr**

virus-related cross reactive autoimmune response in multiple sclerosis in Norway

AUTHOR(S): Vaughan, J. H.; Riise, T.; Rhodes, G. H.; Nguyen, M.-D.; Barrett-Connor, E.; Nyland, H.

CORPORATE SOURCE: Department of Medicine-0663 and The Sam and Rose Stein Institute for Research on Aging, University of California, San Diego, La Jolla, CA, 92093, USA

SOURCE: J. Neuroimmunol. (1996), 69(1-2), 95-102
CODEN: JNRIDW; ISSN: 0165-5728

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In studies of patients in Norway with multiple sclerosis (MS), we have found cross reactive autoantibodies related to the **Epstein Barr** virus nuclear antigen-1 (EBNA-1). The MS patients had elevated IgG antibody to EBNA-1, as measured by reactivity with a synthetic glycine/alanine peptide, P62, which represents the glycine/alanine repeat in EBNA-1. The mean titer of anti-P62 in patients with acute relapse at the time of **assay** was significantly higher than in the remaining patients. Patients with remitting/relapsing MS also had elevated autoantibody to a lymphocyte protein, p542, cross reactive with EBNA-1 through a glycine/serine epitope. High titered anti-EBNA-1 antibodies from some MS, as well as from some **SLE** sera, were shown to cross react with 80-82 kDa and 60 kDa proteins in neuroglial cells.

L22 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1995:766386 CAPLUS

DOCUMENT NUMBER: 123:254320

TITLE: Reduced expression of peptide-loaded HLA class I molecules on multiple sclerosis lymphocytes

AUTHOR(S): Li, Fangqin; Linan, Mercedes J.; Stein, Marion C.; Faustman, Denise L.

CORPORATE SOURCE: Immunobiology Laboratories, Massachusetts General Hospital, Charlestown, MA, USA

SOURCE: Ann. Neurol. (1995), 38(2), 147-54
CODEN: ANNED3; ISSN: 0364-5134

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lymphocytes from patients with HLA class II-linked autoimmune diseases such as type I diabetes, **systemic lupus** erythematosus, rheumatoid arthritis and Graves' have recently been shown to have a decrease in the expression of self-peptide-filled HLA class I antigens on the surface of peripheral lymphocytes. The human demyelinating diseases of multiple sclerosis in some cases are also assocd. with the presence of certain HLA class II genes, which may in turn be linked to genes in the class II region that control class I expression. Hence, we studied fresh peripheral blood mononuclear cells (PBMCs) and newly produced **Epstein-**

Barr virus (**EBV**)-transformed cell lines from multiple sclerosis patients for the class I defect. Unsepd. PBMCs, as well as T cells, B cells, and macrophages from multiple sclerosis patients had a decrease in the amt. of conformationally correct peptide-filled HLA class I mols. on the cell surface compared with matched controls **detectable** by flow cytometry. To demonstrate the independence of this defect from exogenous serum factors, newly produced **EBV**-transformed cell lines from B cells of patients with multiple sclerosis maintained the defect. In addn., DR2 +/+, +/-, and -/- **EBV**-transformed B cells from these patients similarly demonstrated the self-antigen presentation defect. Anal. of a set of discordant multiple sclerosis twin revealed the class I defect was exclusively found on the affected twin lymphocytes, suggesting a role of this class I complex in disease expression. These data indicate that multiple sclerosis patients have abnormal presentation of self-antigen. This phenomen, common to a no. of HLA-linked autoimmune disorders, may be assocd. with failed self-tolerance and improper T-cell education secondary to faulty HLA class I assembly controlled by HLA class II linked genes.

L22 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:78925 CAPLUS
DOCUMENT NUMBER: 122:130584
TITLE: Production and nucleotide sequence of an inhibitory human IgM autoantibody directed against platelet glycoprotein Ia/IIa
AUTHOR(S): Deckmyn, H.; Zhang, J.; Van Houtte, E.; Vermylen, J.
CORPORATE SOURCE: Center Molecular Vascular Biology, Louvain, B-3000, Belg.
SOURCE: Blood (1994), 84(6), 1968-74
CODEN: BLOOAW; ISSN: 0006-4971
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human B-cell lines were derived by limiting dilns. of **Epstein-Barr** virus (**EBV**) transformed peripheral B cells from a patient with an autoantibody against glycoprotein (GP)Ia/IIa, and manifesting defective collagen-induced platelet aggregation and a bleeding problem. Antibody-producing clones were selected for their reactivity with whole platelets or with affinity-purified GPIa/IIa by ELISA. One of these cell lines, selected for further evaluation, produced an IgM (E3G6) that interfered with platelet aggregation responses. Polymerase chain reaction (PCR) amplifications with two different sets of primers specific for human .kappa.-chains resulted in the rescue of a unique and identical sequence. The same was true for the .mu.-chain, from which it was concluded that the cell line was monoclonal. Further anal. showed that the .kappa. variable domain sequence is similar to

the germline gene A30, to 2E7, an anti-GPIIb human autoantibody, and to HF2-1/17, a **systemic lupus** erythematosus (**SLE**)-assocd. broad-specificity human autoantibody. Thus, the specificity of the antibody, E3G6, appears to be **detd.** by the .mu.-chain, the sequence of which is encoded by a VHIII gene segment strongly homologous to the germline gene DP-77, by a D gene that is not homologous to any of the germline D genes reported to date, and by JH4 gene segment that is germline. All four mutations vs. DP-77 are in CDRs, and result in amino acid substitutions, which implies that E3G6 may have been derived from an antigen-driven response.

L22 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1994:698651 CAPLUS
DOCUMENT NUMBER: 121:298651
TITLE: A 16mer peptide of the human autoantigen calreticulin is a most prominent HLA-DR4Dw4-associated self-peptide
AUTHOR(S): Max, Heiner; Halder, Thomas; Kalbus, Matthias; Gnau, Volker; Jung, Gunther; Kalbacher, Hubert
CORPORATE SOURCE: Medicine and Natural Sciences Research Center, University Tubingen, Tuebingen, 72074, Germany
SOURCE: Hum. Immunol. (1994), 41(1), 39-45
CODEN: HUIMDQ; ISSN: 0198-8859
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The human Ca2+-binding (storage) protein calreticulin, located in the lumen of the endoplasmic reticulum, is proposed to play a role as autoantigen: anti-calreticulin autoantibodies occur in the sera of patients with **SLE** and patients with onchocerciasis (calreticulin shows a high sequence homol. to the Onchocerca volvulus antigen RAL-1). Here the authors present sequencing data of a HLA-DR4Dw4-assocd. calreticulin peptide fragment, Cal(295-310), purified from a DR4Dw4 self-peptide pool. Cal(295-310) proved to be one of three commonest self-peptides assocd. with DR4Dw4 mols. that were isolated from the **EBV**-transformed B-cell line BSM (DR4Dw4, DRw53). The authors tested the binding of Cal(295-309) and the analogous RAL-1 peptide to HLA-DR mols.: Cal(295-309) exhibited specific binding characteristics for DR4Dw4. Binding **assays** using self-peptide analogs with replaced amino acids led the authors to a DR4Dw4-binding motif with anchor residues at relative positions 1 and 6. The sequencing data suggest that calreticulin is a frequently processed intracellular protein. The abundance of calreticulin makes the presentation of different calreticulin peptides assocd. with HLA-D mols. likely to occur, supporting the immunol. relevance of this mol.

L22 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1994:653484 CAPLUS

DOCUMENT NUMBER: 121:253484
TITLE: Heterogeneity and diversity of IgM and IgG lupus anticoagulants in an individual with **systemic lupus** erythematosus
AUTHOR(S): Nakamura, Norihiko; Azuma, Chihiro; Akamizu, Takashi; Sugawa, Hideo; Matsuda, Fumihiko; Mitsuda, Nobuaki; Honjo, Tasuku; Mori, Toru; Yamaji, Kenji
CORPORATE SOURCE: Fac. Med., Osaka Univ., Toyonaka, 560, Japan
SOURCE: Biochem. Biophys. Res. Commun. (1994), 203(3), 1789-94
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB From one patient with **systemic lupus** erythematosus retaining lupus anticoagulant (LAC), 6 **Epstein -Barr** virus-transformed human B cell clones secreting antibodies that affect the coagulation **assay** were established. Two and 4 of the clones secreted IgM and IgG antibodies, resp. Although all 6 antibodies displayed anticardiolipin activity in ELISA, the increased binding activity in the presence of .beta.2-glycoprotein I was limited only to the IgG antibodies. Five antibodies (two IgM and three IgG) had LAC activity which prolonged the activated partial thromboplastin time (APTT), whereas one IgG antibody shortened the APTT. Two of the IgG producing clones had an identical Ig heavy chain gene rearrangement despite their opposite effects on the coagulation **assay**. These results demonstrated the heterogeneity of LACs and diversity among their physiol. functions.

L22 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1994:555036 CAPLUS
DOCUMENT NUMBER: 121:155036
TITLE: Soluble Fc.epsilon.RII/CD23 in patients with autoimmune diseases and **Epstein-Barr** virus-related disorders: Analysis by ELISA for soluble Fc.epsilon.RII/CD23
AUTHOR(S): Yoshikawa, Tsutomu; Nanba, Toshihiko; Kato, Hironori; Hori, Kotaro; Inamoto, Takashi; Kumagai, Shunichi; Yodoi, Junji
CORPORATE SOURCE: Department Biological Responses, Institute Virus Research, Sakyo, 606-01, Japan
SOURCE: ImmunoMethods (1994), 4(1), 65-71
CODEN: IMUME8; ISSN: 1058-6687
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The low-affinity Fc receptor for IgE (Fc.epsilon.RII/CD23) and its sol. form (sCD23, IgE-binding factor) have multiple functions, and enhanced levels of these are assocd. with various immunol. diseases.

The authors established two sensitive ELISA systems using enzyme-conjugated mAb and biotinylated mAb. The **detection** limits of the ELISA systems were 0.03 and 1.0 ng/mL, which showed good correlation in the range 1.0-10 ng/mL. In the ELISA system using enzyme-conjugated mAb, the av. sCD23 concn. in 303 normal healthy volunteers was 1.4 .+-. 0.3 ng/mL. In the ELISA system using biotinylated mAb, sCD23 levels in normal healthy volunteers showed almost the same values. In patients with autoimmune diseases such as rheumatoid arthritis, **systemic lupus** erythematosus, Sjogren syndrome, progressive systemic sclerosis, and mixed connective tissue disease, the sCD23 levels were significantly higher than those in normal individuals. Furthermore, in **Epstein-Barr** virus-related disorders after liver transplantation with immunosuppression, plasma levels of sCD23 rapidly increased to more than 12 ng/mL when clin. symptoms were evident. In addn., the sCD23 values remained high, although elevated GOT levels gradually decreased to std. values and **EBV** hepatitis improved. These data suggest that sCD23 levels are a sensitive marker to autoimmune diseases and **EBV** -related disorders in addn. to allergic disorders. The ELISA system for sCD23 may be an addnl. **diagnostic** tool in estg. the clin. courses of these diseases.

L22 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1994:268017 CAPLUS
DOCUMENT NUMBER: 120:268017
TITLE: Human Rheumatoid Factors with Restrictive Specificity for Rabbit Immunoglobulin G: Auto- and Multi-reactivity, Diverse VH Gene Segment Usage and Preferential Usage of V.lambda.IIIb
AUTHOR(S): Fang, Qiang; Kannapell, Carol C.; Gaskin, Felicia; Solomon, Alan; Koopman, William J.; Fu, Shu Man
CORPORATE SOURCE: Sch. Med., Univ. Virginia, Charlottesville, VA, 22908, USA
SOURCE: J. Exp. Med. (1994), 179(5), 1445-56
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To **det**. the mol. and functional properties of human rheumatoid factors (RF), the authors established stable hybridomas and **Epstein-Barr** virus-transformed B cell lines from the synovial fluid or peripheral blood of three patients with rheumatoid arthritis and one patient with **systemic lupus** erythematosus. 17 Cell lines were obtained that produced high-titer Ig M (IgM) RF that reacted exclusively with rabbit but not human IgG or IgG of other mammalian species. Certain anti-rabbit IgG RF also had specificity for other mammalian antigens (Ag), including cytoskeletal proteins and intracellular proteins

found in HeLa cells, as well as for Ag present in an ext. prepd. from the cell wall of group A streptococci. 13 Of the 17 RF contained .lambda.-type light (L) chains, of which 12 were classified serol. as members of the .lambda.-L chain variable region (V.lambda.) subgroup, designated V.lambda.III. The heavy chain V region (VH) and V.lambda. sequences of nine of these IgM.lambda. RF were **detd**. at the cDNA level. Five VH genes in three VH families were used by these antibodies (Ab), including VH1 (dp21/1-4b and dp10 [51p1]/hv1051), VH3 (dp38/3-15 and dp77/13-21), and VH4 (dp70/4-4b). The deduced V gene-encoded amino acid sequences of the .lambda. chains of these IgM.lambda. RF confirmed their serol. classification as .lambda.III, and they were further classified as members of the relatively uncommon V.lambda.III subgroup, designated V.lambda.IIIb. Based on cDNA analyses, nine were the product of three V.lambda.IIIb germline genes. Two such genes, designated hsiggll150 and hsiggll295, were cloned and sequenced from genomic DNA. Unique combinations of these VH and V.lambda.IIIb genes could be related to distinctive patterns of reactivity among the IgM.lambda. RF. Although the VH and V.lambda. regions of these Abs were expressed primarily as germline-encoded sequences, four of nine multireactive Abs had extensive V region mutation, indicative of an Ag-driven process. The finding that .lambda.IIIb L chains are preferentially found among anti-rabbit IgG RF, and that some of these Ab have specificity for other protein, cellular, and bacterial Ag, provides new insight into the pathogenesis of RA and related diseases.

L22 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:407069 CAPLUS
DOCUMENT NUMBER: 119:7069
TITLE: Autoantibodies from patients with **systemic lupus** erythematosus bind a shared sequence of SmD and **Epstein-Barr** virus-encoded nuclear antigen EBNA I
AUTHOR(S): Sabbatini, Alessandra; Bombardieri, Stefano; Migliorini, Paola
CORPORATE SOURCE: Clin. Immunol. Unit, Univ. Pisa, Pisa, Italy
SOURCE: Eur. J. Immunol. (1993), 23(5), 1146-52
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB SmD is one of the small nuclear ribonucleoproteins frequently targeted by autoantibodies in **systemic lupus** erythematosus. The authors isolated and characterized the antibodies present in lupus sera that are specific for the C-terminal region of SmD (sequence 95-119). This region is highly homologous to sequence 35-58 of the EBNA I antigen, one of the nuclear antigens induced by infection with **Epstein-**

Barr virus. Antibodies affinity purified over a peptide 95-119 column were able to recognize this sequence in the context of the whole SmD mol., as they reacted with blotted recombinant SmD. Anti-SmD 95-119 antibodies bound also the EBNA I 35-58 peptide and **detected** the EBNA I mol. in a total cell ext. from **Epstein-Barr** virus-infected lines. A population of anti-SmD antibodies is, therefore, able to bind an epitope shared by the autoantigen and the viral antigen EBNA I. To investigate the involvement of this shared epitope in the generation of anti-SmD antibodies, the authors immunized mice with the EBNA I 35-58 peptide. Sera from immunized animals displayed the same pattern of reactivity of spontaneously produced anti-SmD antibodies. They reacted in fact with the EBNA peptide as well as with SmD 95-119 and recombinant SmD. These data suggest that mol. mimicry may play a role in the induction of anti-SmD autoantibodies.

L22 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1992:488471 CAPLUS
DOCUMENT NUMBER: 117:88471
TITLE: Clonal frequency analysis of B cells producing pathogenic anti-DNA antibody-associated idiotypes in **systemic lupus** erythematosus
AUTHOR(S): Shibata, Shinobu; Sasaki, Takeshi; Hatakeyama, Akira; Munakata, Yasuhiko; Hirabayashi, Yasuhiko; Yoshinaga, Kaoru
CORPORATE SOURCE: Sch. Med., Tohoku Univ., Sendai, 980, Japan
SOURCE: Clin. Immunol. Immunopathol. (1992), 63(3), 252-8
CODEN: CLIIAT; ISSN: 0090-1229
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In order to identify the mechanism responsible for autoantibody prodn. in **systemic lupus** erythematosus (**SLE**), B cell repertoires assocd. with anti-DNA idiotypes were explored by a limiting diln. anal. using **Epstein-Barr** virus (**EBV**) transformation methods and ELISA spot **assays**. The frequencies of B cell clones producing antibodies to DNA and to conventional antigens, tetanus toxoid, dinitrophenyl, or keyhole limpet hemocyanin were higher in active **SLE** compared to those in inactive **SLE** and in normal subjects. In addn., there was a disproportionate increase in anti-DNA antibody- and anti-DNA idiotype (Id)-producing clones at the precursor cell levels as well as at the mature cell level. On the other hand, nos. of anti-Id clones against anti-DNA-Id, termed 0-81 Id, were markedly increased at inactive stages of the disease but not at active stages. These were confirmed by serial studies in some patients with **SLE**. These results support a two-step mechanism for autoantibody prodn., in which initial polyclonal

activation is followed by an antigen-driven process, and indicate an alteration of the precursor B cell repertoire in **SLE**, which may also assoc. with a preferential expansion of anti-DNA clones.

L22 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1991:653780 CAPLUS
DOCUMENT NUMBER: 115:253780
TITLE: Molecular characteristics of antibodies bearing an anti-DNA-associated idiotype
AUTHOR(S): Manheimer-Lory, Audrey; Katz, Jessica B.; Pillinger, Michael; Ghossein, Cybele; Smith, Alan; Diamond, Betty
CORPORATE SOURCE: Dep. Microbiol. Immunol., Albert Einstein Coll. Med., Bronx, NY, 10461, USA
SOURCE: J. Exp. Med. (1991), 174(6), 1639-52
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Anti-double-stranded DNA antibodies are the hallmark of the disease **systemic lupus** erythematosus and are believed to contribute to pathogenesis. While a large no. of anti-DNA antibodies from mice with lupus-like syndromes have been characterized and their variable region genes sequenced, few human anti-DNA antibodies have been reported. Here are described the variable region gene sequences of 8 antibodies produced by **Epstein-Barr** virus (**EBV**)-transformed B cells that bear the 3I idiotype, an idiotype expressed on anti-DNA antibodies and present in high titer in patients with **systemic lupus**. The comparison of these antibodies to the light chains of 3I+ myeloma proteins and serum antibodies reveals that **EBV** transformation yields B cells producing antibodies representative of the expressed antibody repertoire. The anal. of nucleotide and amino acid sequences of these antibodies suggests the first complementarity **detg**. region for the light chain may be important in DNA binding and that paradigms previously generated to account for DNA binding require modification. The understanding of the mol. genetics of the anti-DNA response requires a more complete description of the immunoglobulin germ line repertoire, but data reported here suggest that somatic diversification is a characteristics of the anti-DNA response.

L22 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1991:427352 CAPLUS
DOCUMENT NUMBER: 115:27352
TITLE: Generation and analysis of clonal IgM- and IgG-producing human B cell lines expressing an anti-DNA-associated idiotype

AUTHOR(S): Manheimer-Lory, Audrey J.; Davidson, Anne; Watkins, Dorothy; Hannigan, Noreen R.; Diamond, Betty A.
CORPORATE SOURCE: Dep. Microbiol. Immunol., Albert Einstein Coll. Med., Bronx, NY, 10461, USA
SOURCE: J. Clin. Invest. (1991), 87(5), 1519-25
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study describes a methodol. for generating stable, cloned, **EBV**-transformed IgG- and IgM-producing human B cell lines. Using these lines the authors characterized Ig V gene utilization in an anti-DNA-assocd. idiotype system. The 3I anti-DNA-assocd. idiotype is encoded preferentially by the VK1 gene family, and, in all probability, reflects a germ line gene-encoded framework **determinant**. Anal. of these lines indicates that the DNA-binding antibodies produced by B cell lines from **SLE** patients may differ from DNA binding myeloma proteins and from natural autoantibodies.

L22 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1989:437734 CAPLUS
DOCUMENT NUMBER: 111:37734
TITLE: **Detection** of antibodies to the antigens involving differentiation of myeloid cells in sera from patients with **systemic lupus** erythematosus
AUTHOR(S): Kitagawa, Harukazu; Hoshino, Takashi
CORPORATE SOURCE: Dep. Immunol. Parasitol., Fukui Med. Sch., Fukui, 910-11, Japan
SOURCE: Immunol. Lett. (1989), 21(3), 227-35
CODEN: IMLED6; ISSN: 0165-2478
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The sera from patients with **systemic lupus** erythematosus (**SLE**) were examd. by the immunoblotting method to **detect** antibodies to the antigens on the cultured myeloid cell lines, fresh monocytes, and granulocytes. The sera from **SLE** patients demonstrated antibodies to many antigens on myeloid cells at high frequencies. In particular, the sera from **SLE** patients were found to contain the antibody to the antigens with mol. wt. of 60K on K562, KG-1, and HL60 cells, which are known to express a good amt. of c-myc products. The sera from healthy controls demonstrated hardly any antibody to the 60K antigen on HL60 cells. After an incubation of HL60 cells with TPA or vitamin D3 to induce their monocytic differentiation, the **SLE** sera became able to **detect** the 55K antigen on the differentiated HL60 cells, while the 60K antigen became undetecatable. Thus, the 60K antigen on HL60 cells may be related

to a gene product involving cell growth or differentiation, such as c-myc protein. Actually, polyclonal antibody to myc-specific peptide could identify the 60K antigen as one of the cellular products of HL60. The **SLE** sera contg. the antibody to the 60K antigen on HL60 cells were able to recognize antigens on Raji cells which are known to be c-myc-related proteins and the **EB** virus nuclear antigen (EBNA) subtypes 1, 2, 3 and 4, resp. Apparently, the **SLE** sera possibly contain antibodies to several oncogene products. The pathogenetical role of the antibody to c-myc-related protein in **SLE** is discussed.

L22 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1987:194351 CAPLUS
DOCUMENT NUMBER: 106:194351
TITLE: Human lymphocytes making rheumatoid factor and antibody to ssDNA belong to Leu-1+ B-cell subset
AUTHOR(S): Casali, Paolo; Burastero, Samuele E.; Nakamura, Minoru; Inghirami, Giorgio; Notkins, Abner Louis
CORPORATE SOURCE: Lab. Oral Med., Natl. Inst. Dent. Res., Bethesda, MD, 20892, USA
SOURCE: Science (Washington, D. C., 1883-) (1987), 236(4797), 77-81
CODEN: SCIEAS; ISSN: 0036-8075
DOCUMENT TYPE: Journal
LANGUAGE: English
AB B lymphocytes bearing the Leu-1 cell-surface antigen (Leu-1+), the human equiv. of mouse Ly-1+ B lymphocytes, have been **detected** in human peripheral blood, but there is little information on their frequency and properties. Anal. by fluorescence-activated cell sorter and double immunofluorescence showed that Leu-1+ B cells are consistently present in the peripheral blood and spleens of healthy subjects and constitute 17.0% and 17.3%, resp., of total B cells. When purified Leu-1+ and Leu-1- B lymphocytes were transformed into Ig-secreting cells by infection with **Epstein-Barr** virus and the culture fluids were tested for reactivity with self-antigens, at least 2 important autoantibodies, antibody to the Fc fragment of human IgG (rheumatoid factor) and antibody to single-stranded DNA, were found to be made exclusively by Leu-1+ B cells. Thus, the Leu-1+ lymphocytes represent a major subset of the normal human B cell repertoire and include the B cells capable of making autoantibodies similar to those found in **systemic lupus** erythematosus and rheumatoid arthritis.

L22 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1986:607419 CAPLUS
DOCUMENT NUMBER: 105:207419
TITLE: Reactions of sera from patients with rheumatoid arthritis, **systemic lupus**

erythematosus and infectious mononucleosis to **Epstein-Barr** virus-induced polypeptides

AUTHOR(S): Sculley, D. G.; Sculley, T. B.; Pope, J. H.

CORPORATE SOURCE: Queensland Inst. Med. Res., Brisbane, 4006, Australia

SOURCE: J. Gen. Virol. (1986), 67(10), 2253-8
CODEN: JGVIAY; ISSN: 0022-1317

DOCUMENT TYPE: Journal

LANGUAGE: English

AB P3HR-1 and Ramos cells induced with sodium butyrate and 12-O-tetradecanoyl phorbol 13-acetate were used in the protein immunoblot technique to identify **Epstein-Barr** virus (**EBV**)-specific antibodies present in sera from clin. normal individuals and patients with **systemic lupus** erythematosus (**SLE**), rheumatoid arthritis (RA) and infectious mononucleosis (IM). Sixteen **EBV**-specific polypeptides were **detected** ranging in mol. wt. from 22,000 (22K) to 140K. Many of the sera contained antibodies to different subsets of these antigens, and a high proportion expressed autoantibodies which reacted with cellular components from an **EBV** genome-neg. cell line. About 50% of the sera from each category reacted with the 44-48K and 36K and 38K early antigen (EA) components. A high proportion of the **SLE** sera (64%) were found to contain anti-EA antibodies, suggesting an assocn. between **EBV** and **SLE**. Almost all of the **EBV**-seropos. sera examd. contained antibodies against a 22K late antigen, but none of the sera from IM patients reacted with this polypeptide.

L22 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1982:50218 CAPLUS

DOCUMENT NUMBER: 96:50218

TITLE: The isolation of the antibody moieties of immune complexes from serum by the pepsin digestion of conglutinin-anti-conglutinin complexes

AUTHOR(S): Lachmann, P. J.; Macanovic, M.; Harkiss, G. D.; Oldroyd, R. G.; Habicht, J.

CORPORATE SOURCE: MRC Unit Mech. Tumour Immunity, MRC Cent., Cambridge, UK

SOURCE: Clin. Exp. Immunol. (1981), 46(2), 250-8
CODEN: CEXIAL; ISSN: 0009-9104

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A technique is described which allows the antibodies of circulating immune complexes to be isolated as their F(ab')2 fragments. The method is based on the pptn. of the complexes by the sequential addn. of conglutinin and anti-conglutinin, and the subsequent digestion of these ppts. by pepsin. Using this technique it has

been possible to show antibodies to **Epstein-Barr** (**EB**) virus antigens in the immune complexes of patients with Burkitt's lymphoma and to microbial antigens in two patients with nephritis. By substituting DNase for pepsin it has also been possible to show antibodies to DNA-contg. nuclear antigens in the serum of patients with **systemic lupus** erythematosus.

L22 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1981:599209 CAPLUS
DOCUMENT NUMBER: 95:199209
TITLE: Striking similarities are exhibited by two small **Epstein-Barr** virus-encoded ribonucleic acids and the adenovirus-associated ribonucleic acids VAI and VAII
AUTHOR(S): Rosa, Margaret D.; Gottlieb, Ellen; Lerner, Michael R.; Steitz, Joan A.
CORPORATE SOURCE: Dep. Mol. Biophys. Biochem., Yale Univ., New Haven, CT, 06510, USA
SOURCE: Mol. Cell. Biol. (1981), 1(9), 785-96
CODEN: MCEBD4; ISSN: 0270-7306
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The nucleotide sequence of the region of the **Epstein-Barr** virus genome that specifies 2 small RNAs, EBER 1 and EBER 2, was **detd**. Both of these RNAs are encoded by the right-hand 1000 base pairs of the EcoRI J fragment of **EBV** DNA. EBER 1 is 166 (167) nucleotides long and EBER 2 is .apprx.172 nucleotides long; the heterogeneity resides at the 3' termini. The EBER genes are sepd. by 161 base pairs and are transcribed from the same DNA strand. In vitro, both EBER genes can be transcribed by RNA polymerase III; sequences homologous to previously identified RNA polymerase III intragenic transcription control regions are present. Striking similarities are therefore apparent both between the EBERs and the 2 adenovirus-assocd. RNAs, VAI and VAII, and between the regions of the 2 viral genomes that specify these small RNAs. VAII RNA as well as VAI RNA and the EBERs exist in ribonucleoprotein complexes which are precipitable by anti-La antibodies assocd. with **systemic lupus** erythematosus. Finally, the binding of proteins(s) from uninfected cells confers antigenicity on each of the 4 virus-encoded small RNAs.

L22 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1979:101679 CAPLUS
DOCUMENT NUMBER: 90:101679
TITLE: The binding of anti-DNA antibodies as measured fluorometrically by ethidium bromide
AUTHOR(S): Shepherd, John D.; Fritzler, Marvin J.; Watson,

J. Ian; Van de Sande, Johan H.
CORPORATE SOURCE: Div. Med. Biochem. Med., Univ. Calgary, Calgary, Alberta, Can.
SOURCE: J. Rheumatol. (1978), 5(4), 391-8
CODEN: JRHUA9; ISSN: 0315-162X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The phenanthridine dye ethidium bromide (**EB**) intercalates with double-stranded DNA (dsDNA) resulting in an enhancement of fluorescence. Single-stranded DNA (ssDNA) does not show this fluorescent enhancement. Purified IgG from patients with **systemic lupus** erythematosus (**SLE**) contg. anti-dsDNA antibodies competes with **EB** for binding to DNA resulting in a decrease in fluorescence. Antibodies which bind ssDNA in the Millipore filter radioimmunoassay displace **EB** from dsDNA showing that antigenic **determinants** are available for binding in the double-stranded mol. This study introduces the **EB assay** and presents a comparison with the Millipore filter **assay**.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:27:30 ON 06 DEC 2000)

L23 378 S L21
L24 5 S L23 AND REAGENT
L25 3 S L24 NOT L18
L26 3 DUP REM L25 (0 DUPLICATES REMOVED)

L26 ANSWER 1 OF 3 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 97:294773 SCISEARCH
THE GENUINE ARTICLE: WT085
TITLE: Clinical relevance of autoantibodies in systemic rheumatic diseases
AUTHOR: Fritzler M J (Reprint)
CORPORATE SOURCE: UNIV CALGARY, FAC MED, 3330 HOSP DR NW, CALGARY, AB T2N 4N1, CANADA (Reprint)
COUNTRY OF AUTHOR: CANADA
SOURCE: MOLECULAR BIOLOGY REPORTS, (JUN 1996) Vol. 23, No. 3-4, pp. 133-145.
Publisher: KLUWER ACADEMIC PUBL, SPUIBOULEVARD 50, PO BOX 17, 3300 AA DORDRECHT, NETHERLANDS.
ISSN: 0301-4851.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 203
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Autoantibodies directed to intracellular antigens are serological hallmarks of systemic rheumatic diseases. Identification of circulating autoantibodies is helpful in establishing the correct

diagnosis, indicating the prognosis and providing a guide to treatment and follow-up. Some autoantibodies are included in **diagnostic** and classification criteria for diseases such as anti-Sm antigen and anti-double-stranded DNA antibodies in **systemic lupus** erythematosus, anti-U1 nuclear ribonucleoprotein antibodies in mixed connective tissue disease, and anti-SS-A/Ro and anti-SS-B/La antibodies in Sjogren's syndrome. Over the past 30 years, the identification of new autoantibody systems was advanced by the initiation or adaptation of novel techniques such as double immunodiffusion to **detect** antibodies to saline-soluble nuclear antigens, extraction-reconstitution and ELISA techniques to **detect** histone and chromatin antibodies, immunoblotting and immunoprecipitation to **detect** a wide range of antibodies directed against naturally occurring and recombinant proteins. These techniques have been made possible by advances in cellular and molecular biology and in turn, the sera from index patients have been important **reagents** to identify novel intracellular macromolecules. This paper will focus on the clinical relevance of several autoantibody systems described by Tan and his colleagues over the past 30 years.

L26 ANSWER 2 OF 3 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1989-078649 [11] WPIDS
DOC. NO. NON-CPI: N1989-060047
DOC. NO. CPI: C1989-034924
TITLE: Monoclonal antibody to glyco-lipid GD1a - used for **diagnosing** e.g. cancer, **systemic lupus** erythematosus and disease of nervous system.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): IWATA, D; SATO, W; SHIMADA, S
PATENT ASSIGNEE(S): (MITK) MITSUI TOATSU CHEM INC
COUNTRY COUNT: 6
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 307186	A	19890315	(198911)*	EN	13
R: DE FR GB					
JP 01067198	A	19890313	(198917)		
US 5192662	A	19930309	(199312)		10
CA 1314246	C	19930309	(199315)		
EP 307186	B1	19940622	(199424)	EN	17
R: DE FR GB					
DE 3850325	G	19940728	(199429)		
JP 07116238	B2	19951213	(199603)		9
JP 08187081	A	19960723	(199639)		10
JP 2635946	B2	19970730	(199735)		10

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 307186	A		EP 1988-308273	19880907
JP 01067198	A		JP 1987-221862	19870907
US 5192662	A		US 1988-241291	19880907
CA 1314246	C		CA 1988-576560	19880906
EP 307186	B1		EP 1988-308273	19880907
DE 3850325	G		DE 1988-3850325	19880907
			EP 1988-308273	19880907
JP 07116238	B2		JP 1987-221862	19870907
JP 08187081	A	Div ex	JP 1987-221862	19870907
			JP 1995-167874	19870907
JP 2635946	B2	Div ex	JP 1987-221862	19870907
			JP 1995-167874	19870907

FILING DETAILS:

PATENT NO	KIND		PATENT NO
DE 3850325	G	Based on	EP 307186
JP 07116238	B2	Based on	JP 01067198
JP 2635946	B2	Previous Publ.	JP 08187081

PRIORITY APPLN. INFO: JP 1987-221862 19870907; JP 1995-167874 19870907

AN 1989-078649 [11] WPIDS

AB EP 307186 A UPAB: 19930923
Anti-ganglioside GDia monoclonal antibody (MAb) MZ is claimed, the antibody being capable of recognising the glycolipid GD1a and incapable of recognising the glycolipids GalCer, LacCer, Gb3, Gb4, GA1, GA2, GM1, GM2, GM3, GD1b, GT1b, GQ1b, Fuc-GM1, nLC4. Also claimed is the hybridoma HbMZ, a fusion prod. of antibody-producing cells derived from a GD1a-immunised mammal and myeloma cells, the hybridoma HbMZ being capable of producing the anti-ganglioside GD1a MAb, MZ. Also claimed is a cell strain HZ-1 formed due to transformation of lymphocytes by **EB** virus infection, the cell strain HZ-1 being capable of producing the antibody MZ.
USE/ADVANTAGE - MAb is specific to GD1a and has a high antibody titre against GD1a. Used for **diagnosing** pathological conditions which elevate the level of GDA1a in the blood, e.g. cancer, **systemic lupus** enythematosus and diseases due to organic injury of the nervous system. MAb can also be used to produce an adsorbent resin using e.g. polystyrene.
0/1

ABEQ US 5192662 A UPAB: 19930923
Antiganglioside GD-1-alpha monoclonal antibody, e.g. MZ-1 (FERM BP-2058), responds to the glycolipid GD-1-alpha but does not bind

with the other glycolipids GalCer, LacCer, Gb-3, Gb-4, GA-1, GA-2, GM-1, GM-2, GM-3, GD-1b, GQ-1b, Fuc-GM-1, nLc-4 and sialosyl-nLc-4.

USE - The new antibody is a **screening reagent** for the **diagnosis** of various cancers, **systemic lupus** erythematosus and pathological conditions of the nervous system arising from organic injury.

0/1

ABEQ EP 307186 B UPAB: 19940803

Anti-ganglioside GD1a monoclonal antibody MZ, an antibody capable of recognizing the glycolipid GD1a, and substantially incapable of recognizing the glycolipids GalCer, LacCer, Gb3, Gb4, GA1, GA2, GM1, GM2, GM3, GD1b, GT1b, GQ1b, Fuc-GM1, nLc4.

Dwg.1/1

L26 ANSWER 3 OF 3 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1986-305392 [47] WPIDS

DOC. NO. NON-CPI: N1986-228303

DOC. NO. CPI: C1986-132413

TITLE: Human monoclonal antibody prodn. from B-lymphocytes - by exposure to purified antigen, infection with **Epstein Barr** virus and opt. fusion with myoloma cells.

DERWENT CLASS: B04 D16 S03

INVENTOR(S): RODER, J C

PATENT ASSIGNEE(S): (TOOH) UNIV QUEENS KINGSTON

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
CA 1212913	A	19861021	(198647)*		28

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
CA 1212913	A	CA 1982-406033	19820625

PRIORITY APPLN. INFO: US 1981-278866 19810629; US 1982-388495 19820614

AN 1986-305392 [47] WPIDS

AB CA 1212913 A UPAB: 19930922

Prodn. of human monoclonal antibodies (MAb) comprises first selecting human B-lymphocytes, able to bind to a selected antigen (Ag), from blood, then exposing them to purified Ag, to produce some antigen-specific B cells. The non-specific cells are killed, and the specific cells then infected with **Epstein-Barr** virus (**EBv**). The **EBV**-infected cells are cloned

(by limiting dilution) on irradiated feeder layers of human blood mononuclear cells and monoclonal which secrete specific MAb recovered. Pref. the required clones are selected by ELISA or immuno-isoelectric focussing.

The lymphocytes are pref. exposed to viral (esp. rabies or hepatitis), cancer or blood gp. rhesus antigens; idiotypes on autoantibodies (esp. those related to rheumatoid arthritis, **systemic lupus** erythematosus, Hashimito's throiditis and multiple sclerosis) or tetanus toxoid.

USE/ADVANTAGE - This method provides relatively high yields of MAb, which are useful therapeutically and as **diagnostic reagents**. It can be applied to antigens of any size.
0/2

(FILE 'MEDLINE' ENTERED AT 15:29:40 ON 06 DEC 2000)

L27 24442 SEA FILE=MEDLINE ABB=ON PLU=ON "AUTOIMMUNE DISEASES"/CT

L28 338 SEA FILE=MEDLINE ABB=ON PLU=ON "EPSTEIN-BARR VIRUS INFECTIONS"/CT

L29 3 SEA FILE=MEDLINE ABB=ON PLU=ON L27 AND L28

L29 ANSWER 1 OF 3 MEDLINE
AN 2000407227 MEDLINE
TI [Autoimmune thrombopenia associated with Epstein-Barr virus infection (letter)].
Trombopenia autoinmune asociada a infeccion por virus de Epstein-Barr.
AU Candel Gonzalez F J; Matesanz David M; Fernandez Diez E; Candel Monserrate I; Villarroel Gonzalez-Elipe P
SO REVISTA CLINICA ESPANOLA, (2000 May) 200 (5) 292-3.
Journal code: RNL. ISSN: 0014-2565.

L29 ANSWER 2 OF 3 MEDLINE
AN 2000161980 MEDLINE
TI Virus-induced immune dysregulation as a triggering factor for the development of drug rashes and autoimmune diseases: with emphasis on EB virus, human herpesvirus 6 and hepatitis C virus.
AU Mizukawa Y; Shiohara T
SO JOURNAL OF DERMATOLOGICAL SCIENCE, (2000 Apr) 22 (3) 169-80. Ref: 75
Journal code: AY9. ISSN: 0923-1811.
AB There are a considerable amount of empirical and theoretic medical literature regarding the possible role of viruses in the development of drug rashes and autoimmune diseases: under these conditions, interactions of viruses with the immune system would serve as an accelerating factor of disease pathogenesis. Recent reports have provided evidence to indicate that immune responses against infections with Epstein Barr (EB) virus and human herpesvirus 6 (HHV-6), which are lymphotropic members of the herpes virus group,

not only aid the direct elimination of the virus but also contribute to a favorable milieu for the initiation or acceleration of drug rashes. Viruses that can persist for the lifetime of the host despite strong immune responses against them, such as EB virus and hepatitis C virus (HCV), would be also relevant to the pathogenesis of autoimmune diseases. HCV has been reportedly associated with a wide variety of dermatoses that, in common, show histologically the lichenoid tissue reaction. Although porokeratosis that manifests lichenoid histopathological features had long been regarded as being associated with immunosuppression, we found that HCV could act as trigger for the development of porokeratosis during states of immunosuppression. Thus, the main purpose of this review is to describe recent work on the etiology of drug rashes and autoimmune disease with special reference to viral infections.

L29 ANSWER 3 OF 3 MEDLINE
AN 1999036340 MEDLINE
TI Systemic lupus erythematosus associated with acute Epstein-Barr virus infection.
AU Dror Y; Blachar Y; Cohen P; Livni N; Rosenmann E; Ashkenazi A
SO AMERICAN JOURNAL OF KIDNEY DISEASES, (1998 Nov) 32 (5) 825-8. Journal code: 3H5. ISSN: 0272-6386.
AB Systemic lupus erythematosus (SLE) is a multisystem disease of unknown origin, characterized by a variety of autoimmune phenomena. Viruses have long been postulated to play a role in its pathogenesis. Several observations suggested a link between Epstein-Barr virus (EBV) and SLE. We describe a 14-year-old girl who presented with acute onset of SLE concurrently with clinical and laboratory findings consistent with EBV-induced infectious mononucleosis (IM). Evidence for acute EBV infection was confirmed by serological studies and detection of specific EBV antigens on kidney biopsy. This close association between EBV and SLE suggests a possible role of the virus in the pathogenesis of SLE in this patient.

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:31:21 ON 06 DEC 2000)

L30 2007 S HARLEY J?/AU
L31 4770 S JAMES J?/AU
L32 898 S KAUFMAN K?/AU
L33 25 S L30 AND L31 AND L32
L34 209 S L30 AND (L31 OR L32)
L35 26 S L31 AND L32
L36 7440 S L30 OR L31 OR L32
L37 53 S (L34 OR L36) AND (EB OR EBV OR EPSTEIN BARR)
L38 70 S L33 OR L35 OR L37
L39 39 DUP REM L38 (31 DUPLICATES REMOVED)

_ Author (s)

L39 ANSWER 1 OF 39 MEDLINE

Searcher : Shears 308-4994

ACCESSION NUMBER: 1999374551 MEDLINE
DOCUMENT NUMBER: 99374551
TITLE: **Epstein-Barr** virus infection may be an environmental risk factor for systemic lupus erythematosus in children and teenagers [letter].
AUTHOR: **Harley J B; James J A**
SOURCE: ARTHRITIS AND RHEUMATISM, (1999 Aug) 42 (8) 1782-3. Journal code: 90M. ISSN: 0004-3591.
PUB. COUNTRY: United States
Letter
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199910
ENTRY WEEK: 19991003

L39 ANSWER 2 OF 39 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.DUPLICATE 1
ACCESSION NUMBER: 2000173366 EMBASE
TITLE: **Epstein-Barr** virus infection may be an environmental risk factor for systemic lupus erythematosus in children and teenagers [3].
AUTHOR: **Harley J.B.; James J.A.**
CORPORATE SOURCE: Dr. J.B. Harley, Dept. of Veterans Affairs Med. Ctr., Univ. of Oklahoma Hlth. Sci. Center, Oklahoma Medical Research Foundation, Oklahoma City, OK, United States
SOURCE: Arthritis and Rheumatism, (1999) 42/8 (1782-1783). Refs: 4
ISSN: 0004-3591 CODEN: ARHEAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
031 Arthritis and Rheumatism
LANGUAGE: English

L39 ANSWER 3 OF 39 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999237980 EMBASE
TITLE: Familial aggregation of lupus and autoimmunity in an unusual multiplex pedigree.
AUTHOR: Sestak A.L.; Shaver T.S.; Moser K.L.; Neas B.R.; **Harley J.B.**
CORPORATE SOURCE: Dr. J.B. Harley, Oklahoma Medical Research Foundation, 825 NE 13th Street, Oklahoma City, OK 73104, United States. john-harley@omrf.ouhsc.edu
SOURCE: Journal of Rheumatology, (1999) 26/7 (1495-1499). Refs: 23
ISSN: 0315-162X CODEN: JRHUA
COUNTRY: Canada
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
031 Arthritis and Rheumatism
Searcher : Shears 308-4994

LANGUAGE: English
SUMMARY LANGUAGE: English
AB Objective. To evaluate an unusual pedigree with 8 members diagnosed with systemic lupus erythematosus (SLE). Methods. Pedigree members were evaluated through questionnaires, interviews, and medical records. Sixty members contributed serum samples for autoantibody analysis. Results. The 8 affected females shared several disease features, including arthritis (8/8), antinuclear antibodies (ANA) (8/8), pleuritis (6/8), malar rash (6/8), photosensitivity (5/8), and nephritis (4/8). A total of 15 of 51 (29%) blood relatives had autoantibodies; 9 had autoimmune disease, including 7 with SLE, one with psoriasis, and one with Sjogren's syndrome. Five of 11 (45%) nonconsanguineous spouses also had autoantibodies; one spouse had SLE, and 2 others had thyroid disease. Among 68 spouses of patients with SLE in other pedigrees, only 9 (13%) had autoantibodies, and none were symptomatic ($p = 0.02$). Conclusion. The high rate of autoimmunity among both blood relatives and nonconsanguineous mates in this unusual pedigree suggests a complex interaction of genetic and environmental factors contributing to disease.

L39 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 2
ACCESSION NUMBER: 1999:336086 CAPLUS
DOCUMENT NUMBER: 131:156667
TITLE: Immunization of mice with human 60-kD Ro peptides results in epitope spreading if the peptides are highly homologous between human and mouse
AUTHOR(S): Scofield, R. Hal; **Kaufman, Kenneth M.**; Baber, Usman; **James, Judith A.**; **Harley, John B.**; Kurien, Biji T.
CORPORATE SOURCE: University of Oklahoma Health Sciences Center, Department of Veterans Affairs Medical Center, and WK Warren Medical Research Institute, Oklahoma Medical Research Foundation, Oklahoma City, OK, 73104, USA
SOURCE: Arthritis Rheum. (1999), 42(5), 1017-1024
CODEN: ARHEAW; ISSN: 0004-3591
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Immunization with peptide fragments of autoantigens may lead to an immune response at both the T and B cell level that is directed not only at the immunogen, but also at the autoantigen from which the peptide came. In addn., a complex multicomponent particle may become the target of this expanded immune response. The purpose of this study was to det. the ability of several different peptides from 60 kDa Ro to induce expansion of the immune response to the Ro/La RNP particle. The authors immunized BALB/c mice with 3 different oligopeptides from human 60 kDa Ro (or, SSA). Animals

immunized with peptides either identical to or differing by only 1 amino acid developed autoimmunity to the entire Ro RNP particle. Animals immunized with a human peptide highly divergent from the corresponding mouse sequence developed an immune response to the immunogen only and showed little evidence of epitope spreading. Furthermore, these mice did not have antibodies that bound the poorly conserved mouse homolog peptide, and the antibody response to this peptide did not include IgG1. These data indicate that B lymphocytes specific for the self-peptide that is homologous to the immunogen are a crit. determinant for spreading of the immune response to other components of self.

REFERENCE COUNT: 39
REFERENCE(S):
(1) Abbas, A; Nature 1996, V383, P787 CAPLUS
(2) Ben-Chetrit, E; J Clin Invest 1989, V83, P1284 CAPLUS
(3) Ben-Chetrit, E; J Exp Med 1988, V167, P1560 CAPLUS
(4) Boire, G; Clin Exp Immunol 1995, V100, P489 CAPLUS
(8) Buyon, J; J Immunol Methods 1990, V129, P207 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 5 OF 39 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 3
ACCESSION NUMBER: 1999:275669 BIOSIS
DOCUMENT NUMBER: PREV199900275669
TITLE: Peptide mimics of a major lupus epitope of SM B/B.
AUTHOR(S): **Harley, J. B. (1)**; Kirby, M. Y. (1); **James, J. A. (1)**; **Kaufman, K. M. (1)**
CORPORATE SOURCE: (1) Oklahoma Medical Research Foundation, Univ. of Oklahoma Health Sciences Center, US Dept. of Veterans Affairs Medical Center, Oklahoma City, OK, 73104 USA
SOURCE: FASEB Journal, (March 15, 1999) Vol. 13, No. 5 PART 2, pp. A958.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 99 Washington, D.C., USA April 17-21, 1999 Federation of American Societies for Experimental Biology
. ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English

L39 ANSWER 6 OF 39 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1999:899030 SCISEARCH
THE GENUINE ARTICLE: 242JG
TITLE: Fine specificity mapping of the anti-Sm D2 autoimmune response in SLE patient sera.
AUTHOR: McClain M T (Reprint); **Kaufman K M**; **Harley J B**; **James J A**

Searcher : Shears 308-4994

SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1999) Vol. 42, No. 9, Supp. [S], pp. 250-250.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L39 ANSWER 7 OF 39 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999:531495 BIOSIS
DOCUMENT NUMBER: PREV199900531495
TITLE: Fine specificity mapping of the anti-Sm D2 autoimmune response in SLE patient sera.
AUTHOR(S): McClain, Micah T. (1); **Kaufman, Kenneth M.** (1); **Harley, John B.** (1); **James, Judith A.** (1)
CORPORATE SOURCE: (1) Oklahoma City, OK USA
SOURCE: Arthritis & Rheumatism, (Sept., 1999) Vol. 42, No. 9 SUPPL., pp. S112.
Meeting Info.: 63rd Annual Scientific Meeting of the American College of Rheumatology and the 34th Annual Scientific Meeting of the Association of Rheumatology Health Professionals Boston, Massachusetts, USA November 13-17, 1999
ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L39 ANSWER 8 OF 39 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 4
ACCESSION NUMBER: 1998:490661 CAPLUS
DOCUMENT NUMBER: 129:135181
TITLE: Diagnostics and therapy of **Epstein-Barr** virus in autoimmune disorders
INVENTOR(S): **Harley, John B.**; **James, Judith A.**
PATENT ASSIGNEE(S): Oklahoma Medical Research Foundation, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9830586	A2	19980716	WO 1998-US342	19980113
WO 9830586	A3	19981217		

Searcher : Shears 308-4994

W: AU, CA, JP
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AU 9860185	A1	19980803	AU 1998-60185	19980113
EP 1007552	A2	20000614	EP 1998-903405	19980113

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.:	US 1997-781296	19970113
	WO 1998-US342	19980113

AB Data consistent with autoimmune disease being caused by **Epstein-Barr** virus are shown. Based on this evidence, an effective vaccine would prevent the autoimmune disease in those vaccinated, modified or administered so that the vaccine is not itself capable of inducing autoimmune disease. In the case of anti-Sm, structures to be avoided in **Epstein-Barr** virus-derived vaccine have been identified. Differences have been identified in the immune responses to **Epstein-Barr** infection between individuals who develop a specific autoimmune disease and those who do not. These differences are used to distinguish those who are at greater risk for developing specific autoimmune diseases from those who are at lesser risk. Assuming **Epstein-Barr** virus causes autoimmune disease and that **Epstein-Barr** virus remains latent in the patient for life, reactivation of the virus from the latent state is important in generating or maintaining the autoimmune response that culminates in autoimmune disease. Cells infected with latent virus may also encourage autoimmunity. Based on the understanding that reactivation or latency are important to produce or sustain autoimmunity, then therapies directed against **Epstein-Barr** virus will also be effective therapies for the autoimmune manifestations of disease for which **Epstein-Barr** virus is responsible.

L39 ANSWER 9 OF 39 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1998:775662 SCISEARCH
THE GENUINE ARTICLE: 121HD
TITLE: Identification and analysis of peptide determinants of murine monoclonal anti-Sm B/B' autoantibodies
AUTHOR: McClain M T (Reprint); **Kaufman K M**; Koelsch G; **Harley J B**; **James J A**
CORPORATE SOURCE: UNIV OKLAHOMA, MED RES FDN, OKLAHOMA CITY, OK; VET ADM MED CTR, OKLAHOMA CITY, OK
COUNTRY OF AUTHOR: USA
SOURCE: FASEB JOURNAL, (20 MAR 1998) Vol. 12, No. 5, Part 2, Supp. [S], pp. 5293-5293.
Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998.
ISSN: 0892-6638.
DOCUMENT TYPE: Conference; Journal

FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 0

L39 ANSWER 10 OF 39 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1998:771914 SCISEARCH
THE GENUINE ARTICLE: 125AQ
TITLE: **Epstein Barr** virus nuclear antigen-1 immune response differences between systemic lupus erythematosus patients and normal controls
AUTHOR: **James J A (Reprint); Kaufman K M ; Harley J B**
CORPORATE SOURCE: UNIV OKLAHOMA, HLTH SCI CTR, OKLAHOMA MED RES FDN, OKLAHOMA CITY, OK 73104; VET AFFAIRS MED CTR, OKLAHOMA CITY, OK 73104
COUNTRY OF AUTHOR: USA
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1998) Vol. 41, No. 9, Supp. [S], pp. 1656-1656.
Publisher: LIPPINCOTT-RAVEN PUBL, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L39 ANSWER 11 OF 39 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1998:771585 SCISEARCH
THE GENUINE ARTICLE: 125AQ
TITLE: Fine specificity mapping of the anti-Sm D3 autoimmune response in systemic lupus erythematosus.
AUTHOR: McClain M (Reprint); **Kaufman K M; Harley J B; James J A**
CORPORATE SOURCE: US DEPT VET AFFAIRS, MED CTR, OKLAHOMA CITY, OK 73104; UNIV OKLAHOMA, HLTH SCI CTR, OKLAHOMA MED RES FDN, OKLAHOMA CITY, OK 73104
COUNTRY OF AUTHOR: USA
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1998) Vol. 41, No. 9, Supp. [S], pp. 1325-1325.
Publisher: LIPPINCOTT-RAVEN PUBL, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L39 ANSWER 12 OF 39 BIOSIS COPYRIGHT 2000 BIOSIS

ACCESSION NUMBER: 1998:203671 BIOSIS
DOCUMENT NUMBER: PREV199800203671
TITLE: Identification and analysis of peptide determinants of murine monoclonal anti-Sm B/B' autoantibodies.
AUTHOR(S): McClain, M. T.; **Kaufman, K. M.**; Koelsch, G.; **Harley, J. B.**; **James, J. A.**
CORPORATE SOURCE: Univ. Okla., Oklahoma Med. Res. Foundation, VA Med. Cent., Oklahoma City, OK USA
SOURCE: FASEB Journal, (March 20, 1998) Vol. 12, No. 5, pp. A914.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 98, Part II San Francisco, California, USA April 18-22, 1998 Federation of American Societies for Experimental Biology
. ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English

L39 ANSWER 13 OF 39 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1998:771127 SCISEARCH
THE GENUINE ARTICLE: 125AQ
TITLE: Immunization of mice with human 60 kD Ro peptides results in epitope spreading if the peptides are highly homologous between man and mouse.
AUTHOR: Scofield R H (Reprint); Kurian B T; **Kaufman K M**; Baber U; **James J A**; Haraley J B
CORPORATE SOURCE: UNIV OKLAHOMA, HLTH SCI CTR, OKLAHOMA MED RES FDN, VET AFFAIRS MED CTR, OKLAHOMA CITY, OK 73104
COUNTRY OF AUTHOR: USA
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1998) Vol. 41, No. 9, Supp. [S], pp. 867-867.
Publisher: LIPPINCOTT-RAVEN PUBL, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L39 ANSWER 14 OF 39 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:470036 BIOSIS
DOCUMENT NUMBER: PREV199800470036
TITLE: **Epstein Barr** virus nuclear antigen-1 immune response differences between systemic lupus erythematosus patients and normal controls.
AUTHOR(S): **James, Judith A.**; **Kaufman, Kenneth M.**; **Harley, John B.**

CORPORATE SOURCE: Okla. Med. Res. Foundation., Univ. Okla. Health Sciences Cent., Oklahoma City, OK 73104 USA
SOURCE: Arthritis & Rheumatism, (Sept., 1998) Vol. 41, No. 9 SUPPL., pp. S308.
Meeting Info.: 62nd National Scientific Meeting of the American College of Rheumatology and the 33rd National Scientific Meeting of the Association of Rheumatology Health Professionals San Diego, California, USA November 8-12, 1998 American College of Rheumatology
. ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L39 ANSWER 15 OF 39 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:469707 BIOSIS
DOCUMENT NUMBER: PREV199800469707
TITLE: Fine specificity mapping of the anti-SM D3 autoimmune response in systemic lupus erythematosus.
AUTHOR(S): McClain, Micah (1); **Kaufman, Kenneth M.**; **Harley, John B.**; **James, Judith A.**
CORPORATE SOURCE: (1) Oklahoma Med. Res. Foundation, Univ. Oklahoma Health Sci. Cent., Oklahoma City, OK 73104 USA
SOURCE: Arthritis & Rheumatism, (Sept., 1998) Vol. 41, No. 9 SUPPL., pp. S253.
Meeting Info.: 62nd National Scientific Meeting of the American College of Rheumatology and the 33rd National Scientific Meeting of the Association of Rheumatology Health Professionals San Diego, California, USA November 8-12, 1998 American College of Rheumatology
. ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L39 ANSWER 16 OF 39 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1998:770493 SCISEARCH
THE GENUINE ARTICLE: 125AQ
TITLE: **Epstein Barr** virus exposure is associated with adult systemic lupus erythematosus.
AUTHOR: **James J A (Reprint)**; Hall T J; Sestak A L; Bruner G E; Moser K L; **Harley J B**
CORPORATE SOURCE: UNIV OKLAHOMA, HLTH SCI CTR, OKLAHOMA MED RES FDN, OKLAHOMA CITY, OK 73104; VET AFFAIRS MED CTR, OKLAHOMA CITY, OK 73104
COUNTRY OF AUTHOR: USA
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1998) Vol. 41, No. 9, Supp. [S], pp. 233-233.
Publisher: LIPPINCOTT-RAVEN PUBL, 227 EAST

WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L39 ANSWER 17 OF 39 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 5
ACCESSION NUMBER: 1998:681384 CAPLUS
DOCUMENT NUMBER: 130:79985
TITLE: B-cell epitope spreading in autoimmunity
AUTHOR(S): **James, Judith A.; Harley, John B.**
CORPORATE SOURCE: Department of Medicine, University of Oklahoma Health Sciences Center Oklahoma Medical Research, Oklahoma City, OK, USA
SOURCE: Immunol. Rev. (1998), 164, 185-200
CODEN: IMRED2; ISSN: 0105-2896
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 81 refs. How the immune response matures from recognizing a single or a few structures of the antigen to many is an obviously important process. Models of B-cell epitope spreading have been developed in a variety of systems. For example, immunization of animals with PPPGMRPP, one of the earliest B-cell epitopes in the anti-Sm response found in human lupus, leads to anti-spliceosomal autoimmunity and features of lupus. The humoral immune response spreads from PPPGMRPP to other structures of the spliceosome in an apparently reproducible sequence. B-cell epitope spreading has provided the exptl. basis from which a relation between lupus and **Epstein-Barr** virus was suspected. An understanding of B-cell epitope spreading is likely to lead to important principles in basic immunol. and to answers to human disease problems.
REFERENCE COUNT: 81
REFERENCE(S):
(2) Billings, P; J Biol Chem 1984, V259, P12850 CAPLUS
(3) Bockenstedt, L; J Immunol 1995, V154, P3516 CAPLUS
(5) Cole, G; J Immunol 1995, V155, P2841 CAPLUS
(6) Deutscher, S; Proc Natl Acad Sci USA 1988, V85, P9479 CAPLUS
(7) Gaither, K; Protides Biol Fluid Proc Colloq 1985, V33, P413 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 18 OF 39 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:469249 BIOSIS

DOCUMENT NUMBER: PREV199800469249
TITLE: Immunization of mice with human 60 kD Ro peptides results in epitope spreading if the peptides are highly homologous between man and mouse.
AUTHOR(S): Scofield, R. H.; Kurien, B. T.; **Kaufman, K. M.**; Baber, U.; **James, J. A.**; **Harley, J. B.**
CORPORATE SOURCE: Oklahoma Med. Res. Foundation, Univ. Oklahoma Health Sci. Center, Veterans Affairs Med. Center, Oklahoma City, OK 73104 USA
SOURCE: Arthritis & Rheumatism, (Sept., 1998) Vol. 41, No. 9 SUPPL., pp. S177.
Meeting Info.: 62nd National Scientific Meeting of the American College of Rheumatology and the 33rd National Scientific Meeting of the Association of Rheumatology Health Professionals San Diego, California, USA November 8-12, 1998 American College of Rheumatology
. ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L39 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 6
ACCESSION NUMBER: 1998:354044 CAPLUS
DOCUMENT NUMBER: 129:121268
TITLE: Is there a role for **Epstein-Barr** virus in lupus?
AUTHOR(S): **Harley, John B.**; **James, Judith A.**
CORPORATE SOURCE: University of Oklahoma Health Sciences Center, Oklahoma City, OK, 73104, USA
SOURCE: Immunologist (1998), 6(2), 79-83
CODEN: INOLEG; ISSN: 1192-5612
PUBLISHER: Hogrefe & Huber Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 22 refs. discussing lupus autoantibodies, fine specificity in spliceosomal autoimmunity, a peptide-induced model for lupus autoimmunity, and the assocn. of **EBV** with SLE.

L39 ANSWER 20 OF 39 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:468615 BIOSIS
DOCUMENT NUMBER: PREV199800468615
TITLE: **Epstein Barr** virus exposure is associated with adult systemic lupus erythematosus.
AUTHOR(S): **James, Judith A. (1)**; Hall, Teresa J.; Sestak, Andrea L.; Bruner, Gail E.; Moser, Kathy L.; **Harley, John B.**
CORPORATE SOURCE: (1) Okla. Med. Res. Found., Univ. Okla. Health Sci.

Cent., Oklahoma City, OK 73104 USA
SOURCE: Arthritis & Rheumatism, (Sept., 1998) Vol. 41, No. 9 SUPPL., pp. S71.
Meeting Info.: 62nd National Scientific Meeting of the American College of Rheumatology and the 33rd National Scientific Meeting of the Association of Rheumatology Health Professionals San Diego, California, USA November 8-12, 1998 American College of Rheumatology
. ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L39 ANSWER 21 OF 39 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1997:369915 BIOSIS
DOCUMENT NUMBER: PREV199799669118
TITLE: Lupus humoral autoimmunity after short peptide immunization.
AUTHOR(S): **James, Judith A. (1)**; Scofield, R. Hal; **Harley, John B.**
CORPORATE SOURCE: (1) Arthritis Immunol. Program, Oklahoma Med. Res. Foundation, Oklahoma City, OK 73104 USA
SOURCE: Chiorazzi, N. [Editor]; Lahita, R. G. [Editor]; Pavelka, K. [Editor]; Ferrarini, M. [Editor]. Annals of the New York Academy of Sciences, (1997) Vol. 815, pp. 124-127. Annals of the New York Academy of Sciences; B lymphocytes and autoimmunity.
Publisher: New York Academy of Sciences 2 East 63rd Street, New York, New York 10021, USA.
Meeting Info.: Conference Prague, Czech Republic May 21-25, 1996
ISSN: 0077-8923. ISBN: 1-57331-076-X (cloth), 1-57331-077-8 (paper).
DOCUMENT TYPE: Book; Conference
LANGUAGE: English

L39 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 7
ACCESSION NUMBER: 1997:808801 CAPLUS
TITLE: An increased prevalence of **Epstein-Barr** virus infection in young patients suggests a possible etiology for systemic lupus erythematosus
AUTHOR(S): **James, Judith A.**; **Kaufman, Kenneth M.**; Farris, A. Darise; Taylor-Albert, Elizabeth; Lehman, Thomas J. A.; **Harley, John B.**
CORPORATE SOURCE: Department of Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 73104, USA

SOURCE: J. Clin. Invest. (1997), 100(12), 3019-3026
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An unknown environmental agent has been suspected to induce systemic lupus erythematosus (lupus) in man. Prompted by our recent immunochem. findings, we sought evidence for an assocn. between **Epstein-Barr** virus infection and lupus. Because the vast majority of adults have been infected with **Epstein -Barr** virus, we chose to study children and young adults. Virtually all (116 of 117, or 99%) of these young patients had seroconverted against **Epstein-Barr** virus, as compared with only 70% (107 of 153) of their controls (odds ratio 49.9, 95% confidence interval 9.3-1025, P < 0.00000000001). The difference in the rate of **Epstein-Barr** virus seroconversion could not be explained by serum IgG level or by cross-reacting anti-Sm/nRNP autoantibodies. No similar difference was found in the seroconversion rates against four other herpes viruses. An assay for **Epstein-Barr** viral DNA in peripheral blood lymphocytes established **Epstein-Barr** virus infection in the peripheral blood of all 32 of the lupus patients tested, while only 23 of the 32 matched controls were infected (odds ratio > 10, 95% confidence interval 2.53-.infin., P < 0.002). When considered with other evidence supporting a relationship between **Epstein-Barr** virus and lupus, these data are consistent with, but do not in themselves establish, **Epstein-Barr** virus infection as an etiol. factor in lupus.

L39 ANSWER 23 OF 39 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 97:847544 SCISEARCH
THE GENUINE ARTICLE: XY634
TITLE: An etiology for systemic lupus erythematosus.
AUTHOR: **James J A (Reprint); Kaufman K M** ; Farris A D; TaylorAlbert E; Lehman T J A; **Harley J B**
CORPORATE SOURCE: UNIV OKLAHOMA, HLTH SCI CTR, OKLAHOMA MED RES FDN, OKLAHOMA CITY, OK 73104; VET AFFAIRS MED CTR, OKLAHOMA CITY, OK 73104
COUNTRY OF AUTHOR: USA
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1997) Vol. 40, No. 9, Supp. [S], pp. 803-803.
Publisher: LIPPINCOTT-RAVEN PUBL, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English

REFERENCE COUNT: 0

L39 ANSWER 24 OF 39 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:157731 BIOSIS
DOCUMENT NUMBER: PREV199800157731
TITLE: An etiology for systemic lupus erythematosus.
AUTHOR(S): **James, Judith A. (1)**; **Kaufman, Kenneth M.**; Farris, A. Darise; Taylor-Albert, Elizabeth; Lehman, Thomas J. A.; **Harley, John B.**
CORPORATE SOURCE: (1) Univ. Okla. Health Sci. Cent., Oklahoma City, OK 73104 USA
SOURCE: Arthritis & Rheumatism, (Sept., 1997) Vol. 40, No. 9 SUPPL., pp. S165.
Meeting Info.: 61st National Scientific Meeting of the American College of Rheumatology and the 32nd National Scientific Meeting of the Association of Rheumatology Health Professionals Washington, DC, USA November 8-12, 1997 Association of Rheumatology Health Professionals
. ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L39 ANSWER 25 OF 39 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 8
ACCESSION NUMBER: 1997:432545 CAPLUS
DOCUMENT NUMBER: 127:107913
TITLE: Lupus humoral autoimmunity after short peptide immunization
AUTHOR(S): **James, Judith A.**; Scofield, R. Hal; **Harley, John B.**
CORPORATE SOURCE: Arthritis and Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 73104, USA
SOURCE: Ann. N. Y. Acad. Sci. (1997), 815(B Lymphocytes and Autoimmunity), 124-127
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two rabbits were immunized with a peptide derived from the EBNA-1 antigen of **Epstein-Barr** virus that is very similar to a peptide from the Sm B/B' antigen. Both animals mounted an immune response to the peptide of immunization and also initially against the peptide from Sm B/B'. In one animal, these antibodies appear to be cross-reactive with Sm, leading to the capacity to present this autoantigen (via class II) and then to develop lupus autoimmunity. The other animal, however, developed only peptide-specific antibodies and its immune response never became directed against the whole Sm protein. These observations are

consistent with the paradigm previously offered for the crit. events in human lupus from antigenically cross-reactive intact structure to presentation to autoimmunity (J. A. T. James, et al., 1995).

L39 ANSWER 26 OF 39 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 96:744746 SCISEARCH
THE GENUINE ARTICLE: VH883
TITLE: ANTI-SM SERA RECOGNIZE A RECOMBINANT PROTEIN-DERIVED FROM A SMB/B' ALTERNATIVE OPEN READING FRAME
AUTHOR: **KAUFMAN K M (Reprint); JAMES J A ; HARLEY J B**
CORPORATE SOURCE: UNIV OKLAHOMA, HLTH SCI CTR, OKLAHOMA MED RES FDN, US DEPT VET AFFAIRS MED CTR, OKLAHOMA CITY, OK, 73104
COUNTRY OF AUTHOR: USA
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1996) Vol. 39, No. 9, Supp. S, pp. 917.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: No References

L39 ANSWER 27 OF 39 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1996:501523 BIOSIS
DOCUMENT NUMBER: PREV199699223879
TITLE: Anti-SM sera recognize a recombinant protein derived from a SMB/B' alternative open reading frame.
AUTHOR(S): **Kaufman, K. M.; James, J. A.; Harley, J. B.**
CORPORATE SOURCE: Oklahoma Med. Res. Foundation, Univ. Oklahoma Health Sci. Cent., U.S. Dep. Veterans Affairs Med. Cent., Oklahoma City, OK 73104 USA
SOURCE: Arthritis & Rheumatism, (1996) Vol. 39, No. 9 SUPPL., pp. S180.
Meeting Info.: 60th National Scientific Meeting of the American College of Rheumatology and the 31st National Scientific Meeting of the Association of Rheumatology Health Professionals Orlando, Florida, USA October 18-22, 1996
ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L39 ANSWER 28 OF 39 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 9
ACCESSION NUMBER: 1995:936799 CAPLUS
DOCUMENT NUMBER: 123:336572
TITLE: Temperature sensitivity of the keratin cytoskeleton and delayed spreading of

keratinocyte lines derived from **EBS** patients

AUTHOR(S): Morley, S. M.; Dundas, S. R.; **James, J. L.**; Gupta, T.; Brown, R. A.; Sexton, C. J.; Navsaria, H. A.; Leigh, I. M.; Lane, E. B.

CORPORATE SOURCE: Department Anatomy & Physiology, University Dundee, Dundee, DD1 4HN, UK

SOURCE: J. Cell Sci. (1995), 108(11), 3463-71
CODEN: JNCSAI; ISSN: 0021-9533

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Point mutations in the keratin intermediate filament genes for keratin 5 or keratin 14 are known to cause hereditary skin blistering disorders such as epidermolysis bullosa simplex, in which epidermal keratinocytes are extremely fragile and the skin blisters on mild trauma. The authors show that in 2 phenotypically diverse cases of epidermolysis bullosa simplex, the keratin mutations result in a thermoinstability of the intermediate filament cytoskeleton which can be reproducibly demonstrated even in the presence of tissue culture-induced keratins and in conditions where filament fragility is not otherwise obvious. SV40-T antigen and HPV16 (E6.LAMBDA.E7) immortalized keratinocyte cell lines were examd., established from control and epidermolysis bullosa simplex-affected individuals with either severe (Dowling-Meara) or mild (Weber-Cockayne) forms of the disease. In std. tissue culture conditions no significant and consistent abnormality of the keratin cytoskeleton could be demonstrated. However, after thermal stress, a reduced stability of the keratin filaments was demonstrable in the epidermolysis bullosa simplex cell lines, with filaments breaking into aggregates similar to those seen in skin from **EBS** patients. These aggregates were maximal at 15 min after heat shock and the filament network structure was substantially reversed by 60 min. Differences were also seen in the cells during respreading after replating: cells contg. mutant keratins were slower to respread than controls and fine aggregates were seen at the cell margins in the Dowling-Meara derived cell line. Such delays in restoring the normal intermediate filament network after physiol. processes involving cytoskeleton remodelling may render the cells vulnerable to cytolysis in vivo if phys. challenged during this time window. The steady redn. in the mitotic index of the epidermis during the first few years of life could then explain the clin. improvement which is frequently obsd. in growing children.

L39 ANSWER 29 OF 39 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 10

ACCESSION NUMBER: 1995:283302 BIOSIS

DOCUMENT NUMBER: PREV199598297602

TITLE: **EBS** keratinocyte lines show temperature sensitivity and delayed spreading.

AUTHOR(S): Morley, S. M. (1); Dundas, S. (1); **James, J.**

(1); Brown, R. A.; Sexton, C.; Navasaria, H.; Leigh, I. M.; Lane, E. B. (1)
CORPORATE SOURCE: (1) CRC Cell Structure Res. Group, Cancer Res. Campaign Lab., Dep. Anat. Physiol., Med. Sci. Inst., Dundee DD1 4HN UK
SOURCE: Journal of Investigative Dermatology, (1995) Vol. 104, No. 4, pp. 593.
Meeting Info.: Annual Meeting of the Society for Investigative Dermatology Chicago, Illinois, USA May 24-28, 1995
ISSN: 0022-202X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L39 ANSWER 30 OF 39 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1996:36197 BIOSIS
DOCUMENT NUMBER: PREV199698608332
TITLE: Autoepitopes in lupus.
AUTHOR(S): **Harley, John B. (1); James, Judith A.**
CORPORATE SOURCE: (1) Okla. Med. Res. Found., 825 NE Thirteenth St., Oklahoma City, OK 73104 USA
SOURCE: Journal of Laboratory and Clinical Medicine, (1995) Vol. 126, No. 6, pp. 509-516.
ISSN: 0022-2143.
DOCUMENT TYPE: General Review
LANGUAGE: English

L39 ANSWER 31 OF 39 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 11
ACCESSION NUMBER: 1995:345529 CAPLUS
DOCUMENT NUMBER: 122:158385
TITLE: Sequential autoantigenic determinants of the small nuclear ribonucleoprotein Sm D shared by human lupus autoantibodies and MRL lpr/lpr antibodies
AUTHOR(S): **James, J. A.**; Mamula, M. J.; **Harley, J. B.**
CORPORATE SOURCE: Health Sciences Centre, University of Oklahoma, Oklahoma City, OK, USA
SOURCE: Clin. Exp. Immunol. (1994), 98(3), 419-26
CODEN: CEXIAL; ISSN: 0009-9104
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Autoantibodies directed against the Sm proteins of the spliceosome complex are found in approx. 25% of systemic lupus erythematosus (SLE) patient sera. To det. which regions of the Sm D polypeptide are involved in the lupus autoimmune response, binding to overlapping octapeptides of Sm D has been evaluated with sera from nine Sm D-pos. patients, six patients with other autoimmune serol.,

and five normal human sera. Lupus patient sera which are Sm precipitin-pos. bind various combinations of five regions of the peptide. The major antigenic region, Epitope 5 (REAVA(GR)10GGPRR), is bound by eight of nine Sm precipitin-pos. sera tested. This region of Sm D shows significant sequence homol. with **Epstein-Barr** nuclear antigen-1. To det. the fine specificity of the murine Sm response, four unique Sm D MoAbs derived from MRL lpr/lpr mice and three adult anti-Sm-pos. MRL lpr/lpr mouse sera have been analyzed. Two of these monoclonals, KSm 4 and Y12, as well as the MRL lpr/lpr sera tested, show binding with Epitope 5. Another of these monoclonals, KSm 2, binds octapeptides 84-91, DVEPKVKSKKREAVAG, which corresponds to Epitope 4 of this study. Antibodies from SLE patients with autoimmune serol. other than anti-Sm bind the carboxyl glycine-arginine repeat (GR)10 peptides of Sm D. However, none of the antibodies tested from patients who do not have lupus and who have different autoimmune serol. binds any of the Sm D octapeptides. Normal controls did not significantly bind any of the Sm D octapeptides. These results describe two major regions of shared antigenicity of Sm D between sera from SLE patients and MRL lpr/lpr mice, thereby establishing a basis for the cross-species similarity of autoimmunity to the Sm autoantigen in SLE.

L39 ANSWER 32 OF 39 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 94:436507 SCISEARCH
THE GENUINE ARTICLE: NW616
TITLE: PREDICTION ERRORS OF ESTIMATED BREEDING VALUES IN SIRE EVALUATION
AUTHOR: **JAMES J W (Reprint)**
SOURCE: WOOL TECHNOLOGY AND SHEEP BREEDING, (1994) Vol. 42, No. 1, pp. 1-8.
ISSN: 0043-7875.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: AGRI
LANGUAGE: ENGLISH
REFERENCE COUNT: No References Keyed
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Formulae are given for the standard errors of differences between an initial estimated breeding value (**EBV**) and true breeding value, a second **EBV**, and a combined **EBV**. The cases of clean fleece weight percentage and fibre diameter and a range of family sizes are used to illustrate the expected magnitudes of prediction errors. It is pointed out that even if these are larger than often recognised, they are smaller than for sires without progeny tests.

L39 ANSWER 33 OF 39 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 93:288000 SCISEARCH
THE GENUINE ARTICLE: LA277

TITLE: ANTI-RO IN SJOGRENS-SYNDROME AND SYSTEMIC LUPUS-ERYTHEMATOSUS
AUTHOR: **HARLEY J B (Reprint)**; SCOFIELD R H; REICHLIN M
CORPORATE SOURCE: US DEPT VET AFFAIRS MED CTR, OKLAHOMA CITY, OK, 00000; OKLAHOMA MED RES FDN, OKLAHOMA CITY, OK, 73104; UNIV OKLAHOMA HLTH SCI CTR, HLTH SCI CTR, OKLAHOMA CITY, OK, 73190
COUNTRY OF AUTHOR: USA
SOURCE: RHEUMATIC DISEASE CLINICS OF NORTH AMERICA, (MAY 1992) Vol. 18, No. 2, pp. 337-358. ISSN: 0889-857X.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: ENGLISH
REFERENCE COUNT: 99

L39 ANSWER 34 OF 39 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 91:635956 SCISEARCH
THE GENUINE ARTICLE: GP693
TITLE: SYSTEMIC LUPUS-ERYTHEMATOSUS - RNA-PROTEIN AUTOANTIGENS, MODELS OF DISEASE HETEROGENEITY, AND THEORIES OF ETIOLOGY
AUTHOR: **HARLEY J B (Reprint)**; SCOFIELD R H
CORPORATE SOURCE: OKLAHOMA MED RES FDN, ARTHRIT & IMMUNOL PROGRAM, 825 NE 13TH ST, OKLAHOMA CITY, OK, 73104 (Reprint); UNIV OKLAHOMA, HLTH SCI CTR, DEPT MED, OKLAHOMA CITY, OK, 73190; DEPT VET AFFAIRS MED CTR, OKLAHOMA CITY, OK, 00000
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF CLINICAL IMMUNOLOGY, (1991) Vol. 11, No. 6, pp. 297-316.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 180

L39 ANSWER 35 OF 39 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 12
ACCESSION NUMBER: 1989:568347 CAPLUS
DOCUMENT NUMBER: 111:168347
TITLE: Genomic organization and polymorphisms of the human C3d/**Epstein-Barr** virus receptor
AUTHOR(S): Fujisaku, Atsushi; **Harley, John B.**; Frank, Mark Barton; Gruner, Barbara A.; Frazier, Beth; Holers, V. Michael
CORPORATE SOURCE: Arthritis Immunol. Program, Oklahoma Med. Res. Found., Oklahoma City, OK, 73104, USA
SOURCE: J. Biol. Chem. (1989), 264(4), 2118-25
CODEN: JBCHA3; ISSN: 0021-9258
Searcher : Shears 308-4994

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The human C3d/**Epstein-Barr** virus receptor (CR2/CD21) is a 145-kDa protein primarily expressed on mature B lymphocytes. CR2 is a member of the regulators of complement activation (RCA) gene family found on band q32 of chromosome 1. The RCA proteins are characterized by the presence of 60-70 amino acid short consensus repeats (SCR). A full-length CR2 cDNA was cloned and used to identify overlapping cosmid genomic clones. Anal. of CR2 exon-intron junctions revealed the presence of 3 types of exons in the short consensus repeat region of CR2. First, 4 exons each of which encodes 2 SCR are present. Five exons encode a single SCR. Six exons encode SCRs which are split in identical positions. The order of these types of exons is in a repeated array of 4 SCRs, indicating that the contemporary CR2 gene likely evolved from a more primitive gene contg. 4 SCRs. The CR2 full-length cDNA clone was used to find restriction fragment length polymorphisms (RFLPs). Restriction enzyme TaqI generated 2.55- and 2.10-kilobase (kb) polymorphic bands. This RFLP was mapped near the exon contg. the first 2 SCRs. HaeIII digestion generated polymorphic bands of 1.45, 1.55, and 1.75 kb. Two HaeIII 1.45-kb RFLP band maps near the exon contg. the 15th SCR. The TaqI and HaeIII RFLPs will provide tools for the genetic anal. of CR2. The organization of the CR2 gene provides insights into the evolution of human CR2 and the RCA gene family.

L39 ANSWER 36 OF 39 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 13
ACCESSION NUMBER: 1989:324034 BIOSIS
DOCUMENT NUMBER: BR37:26806
TITLE: SPECIFICITIES OF ANTI-RO-SSA ANTIBODIES SECRETED BY **EPSTEIN-BARR** VIRUS TRANSFORMED B CELL LINES.
AUTHOR(S): FU S M; REICHLIN M; GASKIN F; **HARLEY J B**
CORPORATE SOURCE: OKLA. MED. RES. FOUND., OKLAHOMA CITY, OKLA.
SOURCE: NATIONAL MEETING OF THE AMERICAN SOCIETY FOR CLINICAL INVESTIGATION, WASHINGTON, D.C., USA, APRIL 28-MAY 1, 1989. CLIN RES, (1989) 37 (2), 587A.
CODEN: CLREAS. ISSN: 0009-9279.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

L39 ANSWER 37 OF 39 CONFSCI COPYRIGHT 2000 CSA
ACCESSION NUMBER: 95:63622 CONFSCI
DOCUMENT NUMBER: 95-063622
TITLE: **EBS** keratinocyte lines show temperature sensitivity and delayed spreading
AUTHOR: Morley, S.M.; Dundas, S.; **James, J.**; Brown, R.A.; Sexton, C.; Navsaria, H.; Leigh, I.M.; Lane,

E.B.
CORPORATE SOURCE: CRC Cell Structure Res. Group, Cancer Res. Campaign Lab., Dep. Anatomy & Physiology, Med. Sci. Inst., Dundee DD1 4HN, UK
SOURCE: Elsevier Science Publishing Co., 655 Avenue of the Americas, New York, NY 10010, Abstracts available. Paper No. 234.
Meeting Info.: 952 0085: 1995 Annual Meeting of the Investigative Dermatology (9520085). Chicago, IL (USA). 24-28 May 1995. Society for Investigative Dermatology.
DOCUMENT TYPE: Conference
FILE SEGMENT: DCCP
LANGUAGE: English

L39 ANSWER 38 OF 39 CONFSCI COPYRIGHT 2000 CSA
ACCESSION NUMBER: 97:16335 CONFSCI
DOCUMENT NUMBER: 97-028313
TITLE: Kluever-Bucy Syndrome and **Epstein-Barr** virus: Case report
AUTHOR: **Harley, J.P.**; Escobar, N.G.
CORPORATE SOURCE: Marianjoy Rehabilitation Hosp. and Clinics, Wheaton, IL, USA
SOURCE: American Academy of Physical Medicine and Rehabilitation, 1 IBM Plaza, Suite 2500, Chicago, IL 60611, Abstracts available. Poster Paper No. 19.
Meeting Info.: 964 0064: 58th Annual Assembly of American Academy of Physical Medicine and Rehabilitation (9640064). Chicago, IL (USA). 10-13 Oct 1996. Allergan, Inc.; Athena Neurosciences, Inc.; Metronic, Inc., Neurological Division; Rhone-Poulenc Rorer Pharmaceuticals, Inc.; New York University Medical Center, Dept. of Rehabilitation Medicine.
DOCUMENT TYPE: Conference
FILE SEGMENT: DCCP
LANGUAGE: English

L39 ANSWER 39 OF 39 CONFSCI COPYRIGHT 2000 CSA
ACCESSION NUMBER: 97:16336 CONFSCI
DOCUMENT NUMBER: 97-028314
TITLE: Rehabilitation of **Epstein-Barr** virus encephalitis
AUTHOR: Escobar, N.G.; Lewis, S.; **Harley, J.P.**
CORPORATE SOURCE: Marianjoy Rehabilitation Hosp. and Clinics, Wheaton, IL, USA
SOURCE: American Academy of Physical Medicine and Rehabilitation, 1 IBM Plaza, Suite 2500, Chicago, IL 60611, Abstracts available. Poster Paper No. 20.

Meeting Info.: 964 0064: 58th Annual Assembly of American Academy of Physical Medicine and Rehabilitation (9640064). Chicago, IL (USA). 10-13 Oct 1996. Allergan, Inc.; Athena Neurosciences, Inc.; Metronic, Inc., Neurological Division; Rhone-Poulenc Rorer Pharmaceuticals, Inc.; New York University Medical Center, Dept. of Rehabilitation Medicine.

DOCUMENT TYPE: Conference
FILE SEGMENT: DCCP
LANGUAGE: English

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Searcher : Shears 308-4994